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NAME OF THE DOCUMENT

## PATENT SPECIFICATION

**EXHIBIT** 

#### **NEW GENES** TITLE OF THE INVENTION

# DETAILED EXPLANATION OF THE INVENTION

### **CLAIMS**:

- A purified and isolated protein selected from the group consisting of:
- (a) a protein which consists of an amino acid sequence represented by SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 or
- (b) a protein that activates NF-  $\kappa$  B (Nuclear factor kappa B) and consists of an amino acid sequence having at least one amino acid deletion, substitution or addition in an amino acid sequence represented by SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 or 178.
  - A purified and isolated protein that activates NF-  $\kappa\,B$  and comprises an amino acid sequence having at least 95% identity to the protein according to claim 1 over the entire 2. length thereof.
  - An isolated polynucleotide which comprises a nucleotide sequence encoding a 3. protein selected from the group consisting of:
  - (a) a protein which comprises an amino acid sequence represented by SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89,91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 or

- (b) a protein that activates NF-  $\kappa$  B and consists of an amino acid sequence having at least 178; and one amino acid deletion, substitution or addition in an amino acid sequence represented by SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 or 178.
  - An isolated polynucleotide comprising a polynucleotide sequence selected from the group consisting of:
  - (a) a polynucleotide sequence represented by SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175 or 177; and a polynucleotide sequence complementary to said polynucleotide sequence;
    - (b) a polynucleotide sequence encoding a protein that activates NF-  $\kappa$  B and hybridizing with a polynucleotide having the polynucleotide sequence of (a) under stringent conditions;
    - (c) a polynucleotide sequence which encodes a protein that activates NF-  $\kappa$  B and consists of a polynucleotide sequence having at least one nucleotide deletion, substitution or addition in a polynucleotide sequence represented by SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175 or 177.
      - An isolated polynucleotide comprising a nucleotide sequence which encodes a protein that activates NF-  $\kappa$  B and has at least 95% identity to the polynucleotide sequence according to claim 3 over the entire length thereof.

- An isolated polynucleotide comprising a nucleotide sequence which encodes a protein that activates NF-  $\kappa$  B and has at least 95% identity to the polynucleotide sequence according to claim 4 over the entire length thereof.
- A purified and isolated protein encoded by the polynucleotide according to any one 7. of claims 3 to 6.
- A recombinant vector which comprises a polynucleotide according to any one of 8.
- A transformed cell which comprises the recombinant vector according to claim 8. claims 3 to 6. 9.
- A membrane of the cell according to claim 9, when the protein according to claim 10. 1 or 2 is a membrane protein.
- A process for producing a protein comprising, 11.
- (a) culturing a transformed cell comprising the isolated polynucleotide according to any one of claims 3 to 6 under conditions providing expression of the encoded protein; and (b) recovering the protein from the culture.
  - A process for diagnosing a disease or susceptibility to a disease in a subject related to expression or activity of the protein of claim 1, 2 or 7 in a subject comprising:
  - (a) determining the presence or absence of a mutation in the nucleotide sequence encoding said protein in the genome of said subject; and/or
  - (b) analyzing the amount of expression of said protein in a sample derived from said
  - wherein a diagnosis of disease is made when the amount of the protein expressed is more than 2-fold or higher than normal, or half or lower than normal.
  - A method for screening compounds in respect of activity to inhibit or promote NF-13.  $\kappa$  B activation, which comprises the steps of:
  - (a) providing a cell with a gene encoding a protein that activates NF-  $\kappa$  B, and a component that provides a detectable signal associated with activation of NF-  $\kappa$  B;
  - (b) culturing a transformed cell under conditions, which permit the expression of the gene in a transformed cell;
  - (c) contacting the transformed cell with one or more compounds;

- (d) measuring the detectable signal; and
- (e) isolating or identifying as an activator compound a compound that increases said detectable signal 2-fold or higher than normal and/or isolating or identifying as an inhibitor compound a compound that decreases said detectable signal half or lower than normal.
- 14. A process for producing a pharmaceutical composition, which comprises the steps of:
- (a) providing a cell with a gene encoding a protein that activates NF-  $\kappa$  B, and a component capable of providing a detectable signal;
- (b) culturing a transformed cell under conditions, which permit the expression of the gene in the transformed cell;
- (c) contacting the transformed cell with one or more compounds;
- (d) measuring the detectable signal;
- (e) isolating or identifying as an activator compound a compound that increases said detectable signal 2-fold or higher than normal and/or isolating or identifying as an inhibitor compound a compound that decreases said detectable signal half or less than normal; and (f) optimizing the isolated or identified compound as a pharmaceutical composition.
- 15. A kit for screening a compound in respect of activity to inhibit or promote NF-  $\kappa$  B activation, which comprises:
- (a) a cell comprising a gene encoding a protein that activates NF-  $\kappa$  B, and a component that provides a detectable signal upon activation of NF-  $\kappa$  B; and
- (b) reagents for measuring the detectable signal.
- 16. A monoclonal or polyclonal antibody that specifically binds to the protein according to claim 1, 2 or 7.
- 17. A process for producing a monoclonal or polyclonal antibody that specifically binds to the protein according to claim 1, 2 or 7, which comprises administering the protein according to claim 1, 2 or 7 or epitope-bearing fragments thereof to a non-human animal.
- 18. An antisense oligonucleotide complementary to the polynucleotide according to any one of claims 3 to 6, which prevents NF-  $\kappa$  B activator protein expression.
- 19. A ribozyme which inhibits NF-  $\kappa$  B activation by cleavage of RNA that encodes

the protein according to claim 1, 2 or 7, or by cleavage of RNA that encodes some protein of the pathway that leads to I  $\kappa$  B (Inhibitory protein of NF-  $\kappa$  B) degradation.

- 20. A method for treating a disease, which comprises administering to a subject an amount of a compound screened by the process according to claim 13, and/or a monoclonal or polyclonal antibody according to claim 16, and/or an antisense oligonucleotide according to claim 18 and/or a ribozyme according to claim 19 effective to treat a disease selected from the group consisting of inflammation, autoimmune diseases, infectious disease and cancers.
- 21. A pharmaceutical composition produced by the process according to claim 14 as an inhibitor or promoter of NF-  $\kappa$  B activation.
- 22. A pharmaceutical composition according to claim 21 for the treatment of inflammation, autoimmune diseases, cancers or viral infections.
- 23. A method of treating inflammation, autoimmune diseases, cancers and viral infections, which comprises administering a pharmaceutical composition produced by the process according to claim 14 to a patient suffering from a disease associated with NF-  $\kappa$  B activation.
- 24. A pharmaceutical composition according to claim 21 for the treatment of GVHD, dermatosis, IgA nephritis, purpuric nephritis, proliferative nephritides, or fulminant hepatitis.
- 25. A method of treating GVHD, dermatosis, IgA nephritis, purpuric nephritis, proliferative nephritides, or fulminant hepatitis, which comprises administering a pharmaceutical composition produced by the process according to claim 14 to a patient suffering from a disease associated with inhibition of NF-  $\kappa$  B.
- 26. A pharmaceutical composition which comprises a monoclonal or polyclonal antibody according to claim 16 as an active ingredient.
- 27. A pharmaceutical composition which comprises an antisense oligonucleotide according to claim 18 as an active ingredient.
- 28. The pharmaceutical composition according to claim 26 or 27, wherein the target disease is selected from the group consisting of inflammation, autoimmune diseases,

infectious diseases and cancers.

- 29. A method for obtaining a novel gene having a function, which comprises at least the following steps:
- (a) constructing a full-length cDNA library by the oligo-capping method;
- (b) cotransfecting the full-length cDNA and a plasmid containing a factor emitting a signal indicative of the presence of a protein having the function into cells; and
- (c) selecting a plasmid emitting the signal.
- 30. A computer-readable medium on which a sequence data set has been stored, said sequence data set comprising at least one nucleotide sequence selected from the group consisting of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175 and 177, and/or at least one amino acid sequence selected from the group consisting of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 and 178.
- 31. A method for calculating identity to other nucleotide sequences and/or amino acid sequences, which comprises comparing data on a medium according to claim 30 with data of said other nucleotide sequences and/or amino acid sequences.
- 32. An insoluble substrate to which polynucleotides comprising all or part of the nucleotide sequences selected from the group consisting of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173,

175 and 177, are fixed.

33. An insoluble substrate to which polypeptides comprising all or a part of the amino acid sequences selected from the group consisting of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 and 178, are fixed.

#### DETAILED EXPLANATION OF THE INVENTION

#### TECHNICAL FIELD OF THE INVENTION

The present invention relates to a protein capable of activating NF-  $\kappa$  B, a DNA sequence encoding the protein, a method for obtaining the DNA, a recombinant vector containing the DNA, a transformant containing the recombinant vector, and an antibody which specifically reacts with the protein. The present invention also relates to use of the protein, DNA molecule or antibody of the invention in the diagnosis, treatment or prevention of diseases associated with the excessive activation or inhibition of NF-  $\kappa$  B.

The present invention also relates to a method for screening a substance capable of inhibiting or promoting NF-  $\kappa$  B activation by using the protein, DNA, recombinant vector and transformant.

#### DESCRIPTION OF THE RELATED ART

The transcription factor NF-  $\kappa$  B (nuclear factor kappa B) plays an important role in the transcriptional regulation of various genes involved in inflammation and immunological reactions. NF-  $\kappa$  B is a homo- or heterodimer which belongs to the Rel family. In unstimulated conditions, NF-  $\kappa$  B normally resides in the cytoplasm as an inactive form by forming a complex with an I  $\kappa$  B inhibitory protein (Inhibitory protein of NF-  $\kappa$  B) to mask the nuclear transport signal of NF-  $\kappa$  B.

When cytokines such as interleukin (IL)-1 and tumor necrosis factor (TNF)- $\alpha$  stimulate cells, I  $\kappa$  B is phosphorylated by IKK (I  $\kappa$  B kinase) and degraded by the 26S

proteasome through ubiquitination. The released NF-  $\kappa$  B moves to the nucleus, where it binds to the DNA sequence called the NF-  $\kappa$  B binding sequence and induces the transcription of the gene, which is under control of NF-  $\kappa$  B is believed to regulate the expression of genes such as those for immunoglobulins, inflammatory cytokines (e.g., IL-1 and TNF-  $\alpha$ ), interferons and cell adhesion factors. NF-  $\kappa$  B is involved in inflammation and immune responses through the expression induction of these genes.

The inhibition of the function or activation of NF-  $\kappa$  B may inhibit the expression of many factors (proteins) involved in inflammatory or immunological diseases or other diseases such as tumor proliferation. Thus, NF-  $\kappa$  B is a promising target for medicaments against diseases caused or characterized by autoimmunity or inflammation [see e.g., Clinical Chemistry 45, 7-17 (1999); J Clin. Pharmacol. 38, 981-993 (1998); Gut 43, 856-860 (1998); The New England Journal of Medicine 366, 1066-1071 (1997); TiPS 46-50 (1997); The FASEB Journal 9, 899-909 (1995); Nature 395, 225-226 (1998); Science 278, 818-819 (1997); Cell 91, 299-302 (1997)].

Extracellular information is converted into a certain signal, which passes through the cell membrane and goes through the cytoplasm to the nucleus, where it regulates the expression of the target gene and causes cell responses. Therefore the elucidation of the mechanism of intracellular signal transduction from extracellular stimuli to NF-  $\kappa$  B activation is of very important significance, because it provides very important means of developing new medicaments or therapies against autoimmune diseases and diseases exhibiting inflammatory symptoms.

It is believed that the signal transduction pathway from certain cell stimulation to NF-  $\kappa$  B activation includes many steps mediated by various transmitters such as protein kinases. Therefore it is desirable for more efficient drug discovery to identify the transmitters which play a key role in the pathway, and to focus research on the transmitters to establish a new drug-screening method. Some signaling molecules involved in NF-  $\kappa$  B activation have been identified [e.g., IKK, ubiquitination enzymes and the 26S proteasome described above, as well as TNF receptor associated factor 2 (TRAF2) and NF-  $\kappa$  B inducing kinase (NIK)]. However, most of the mechanism of NF-  $\kappa$  B activation remains

unknown, and it has been desired new signaling molecules to be identified and further the NF-  $\kappa$  B activation mechanism to be elucidated.

#### PROBLEM TO BE SOLVED BY THE INVENTION

The object of the present invention is to identify a new gene and protein capable of activating NF-  $\kappa$  B, and to provide a method of use of them in medicaments, diagnostics and therapy. That is, the present invention provides a new protein capable of activating NF-  $\kappa$  B, a DNA sequence encoding the protein, a recombinant vector containing the DNA, a transformant containing the recombinant vector, a process for producing the protein, an antibody directed against the protein or a peptide fragment thereof, and a process for producing the antibody.

The present invention also provides a method for screening a substance capable of inhibiting or promoting NF-  $\kappa$  B activation, a kit for the screening, a substance capable of inhibiting or promoting NF-  $\kappa$  B activation obtainable by the screening method or the screening kit, a process for producing the substance, a pharmaceutical composition containing a substance capable of inhibiting or promoting NF-  $\kappa$  B activation, etc.

#### MEANS TO SOLVE THE PROBLEM

Recently, random analysis of cDNA molecules has been intensively carried out to analyze various genes, which are expressed in vivo. The cDNA fragments thus obtained have been entered for databases and published as ESTs (Expressed Sequence Tags, e.g., http://www.ncbi.nlm.nih.gov/dbEST). However, ESTs are merely sequence information, and it is difficult to predict their functions. ESTs are also arranged in UniGene (http://www.ncbi.nlm.nih.gov/UniGene), and about 92,000 clusters have been registered until now. However, most of these ESTs have their 5' end nucleotide sequences deleted, and contain no translation initiation site. Therefore it is unlikely that such analysis will directly lead to gene functional analysis such as the analysis of protein functions on the assumption of the determination of mRNA coding regions and the understanding of gene expression control by the analysis of promoters.

On the other hand, one method to elucidate functions of gene products (i.e., proteins) is transient expression cloning method using animal cells [see e.g., "Idenshi

Kougaku Handbook (Genetic Engineering Handbook)", an extra issue of "Jikken Igaku (Experimental Medicine)", YODOSHA CO., LTD.]. This method involves transfecting animal cells with a cDNA library constructed using an animal cell expression vector to directly express a functional protein, and identifying and cloning the cDNA based on the biological activity of the protein having an effect on the cells. This method requires no chemical information (amino acid sequences and molecular weights) regarding the target protein product as a prerequisite, and allows the identification of cDNA clones by detecting specific biological activity of the protein expressed in the cells or culture.

For the efficient expression cloning, there is a need to devise a method of preparing a cDNA library. Several methods have been widely used to construct cDNA libraries [e.g., the method of Gubbler-Hoffman: Gene 25 (1983); and the method of Okayama-Berg: Mol. Cell. Biol. 2 (1982)]. However, most of the cDNA molecules prepared by these methods have their 5' end nucleotide sequences deleted, and thus these methods rarely produce full-length cDNA, a complete DNA copy of mRNA. This is because the reverse transcriptase used to prepare cDNA from mRNA does not necessarily have high efficiency in producing full-length cDNA. Therefore it is necessary to improve these prior art methods in order to efficiently carry out the above expression cloning.

In addition, in order to carry out the functional analysis of genes, it is essential to clone full-length cDNA sequences and express proteins from them. Therefore, it has been necessary to construct cDNA libraries containing enriched full-length cDNA for efficient expression cloning.

The present inventors have intensively studied to solve the above problems. As a result, the present inventors have succeeded in constructing a full-length cDNA library by using the oligo-capping method; establishing an assay system using 293EBNA cells; and isolating a new DNA (cDNA) encoding a protein having a function of activating NF-  $\kappa$  B by using the assay system. This new DNA molecule induced NF-  $\kappa$  B activation by its expression in 293EBNA cells. This result shows that this new DNA is a signal transduction molecule involved in NF-  $\kappa$  B activation. Thus, the present invention has been completed.

That is, the present invention relates to:

- (1) A purified and isolated protein selected from the group consisting of:
- (a) a protein that activates NF-  $\kappa$  B which consists of an amino acid sequence represented by SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 or 178; and
- (b) a protein that activates NF-  $\kappa$  B and consists of an amino acid sequence having at least one amino acid deletion, substitution or addition in an amino acid sequence represented by SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89,91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, or 178.
- (2) A purified and isolated protein that activates NF-  $\kappa$  B and comprises an amino acid sequence having at least 95% identity to the protein according to above item (1) over the entire length thereof.
- (3) An isolated polynucleotide which comprises a nucleotide sequence encoding a protein selected from the group consisting of:
- (a) a protein which comprises an amino acid sequence represented by SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 or 178; and
- (b) a protein that activates NF-  $\kappa$  B and consists of an amino acid sequence having at least one amino acid deletion, substitution or addition in an amino acid sequence represented by SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93,

- 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 or 178.
- (4) An isolated polynucleotide comprising a polynucleotide sequence selected from the group consisting of:
- (a) a polynucleotide represented by SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175 or 177; and a polynucleotide sequence complementary to said polynucleotide sequence;
- (b) a polynucleotide sequence encoding a protein that activates NF-  $\kappa$  B and hybridizing with a polynucleotide having the polynucleotide sequence of (a) under stringent conditions; and
- (c) a polynucleotide sequence which encodes a protein that activates NF-  $\kappa$  B and consists of a polynucleotide sequence having at least one nucleotide deletion, substitution or addition in a polynucleotide sequence represented by SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175 or 177.
- (5) An isolated polynucleotide comprising a nucleotide sequence which encodes a protein that activates NF-  $\kappa$  B and has at least 95% identity to the polynucleotide sequence according to above item (3) over the entire length thereof.
- (6) An isolated polynucleotide comprising a nucleotide sequence which encodes a protein that activates NF-  $\kappa$  B and has at least 95% identity to the polynucleotide sequence according to above item (4) over the entire length thereof.
- (7) A purified and isolated protein encoded by the polynucleotide according to any one of above items (3) to (6).

- (8) A recombinant vector which comprises a polynucleotide according to any one of above items (3) to (6).
- (9) A transformed cell which comprises the recombinant vector according to above item (8).
- (10) A membrane of the cell according to above item (9), when the protein according to above item (1) or (2) is a membrane protein.
- (11) A process for producing a protein comprising,
- (a) culturing a transformed cell comprising the isolated polynucleotide according to any one of items (3) to (6) under conditions providing expression of the encoded protein; and
- (b) recovering the protein from the culture.
- (12) A process for diagnosing a disease or a susceptibility to a disease in a subject related to expression or activity of the protein according to above item (1), (2) or (7) in a subject comprising:
- (a) determining the presence or absence of a mutation in the nucleotide sequence encoding said protein in the genome of said subject; and/or
- (b) analyzing the amount of expression of said protein in a sample derived from said subject,

wherein a diagnosis of disease is made when the amount of the protein expressed is 2-fold or higher than normal, or half or lower than normal.

- (13) A method for screening a compound in respect of activity to inhibit or promote NF-  $\kappa$  B activation, which comprises the steps of:
- (a) providing a cell with a gene encoding a protein that activates NF-  $\kappa$  B, and a component that provides a detectable signal associated with activation of NF-  $\kappa$  B;
- (b) culturing a transformed cell under conditions, which permit the expression of the gene in the transformed cell;
- (c) contacting the transformed cell with one or more compounds;
- (d) measuring the detectable signal; and
- (e) isolating or identifying as an activator compound a compound that increases said detectable signal 2-fold or higher than normal and/or isolating or identifying as an inhibitor

compound a compound that decreases said detectable signal half or less than normal.

- (14) A process for producing a pharmaceutical composition, which comprises the steps of:
- (a) providing a cell with a gene encoding a protein that activates NF-  $\kappa$  B, and a component capable of providing a detectable signal;
- (b) culturing a transformed cell under conditions, which permit the expression of the gene in the transformed cell;
- (c) contacting the transformed cell with one or more candidate compounds;
- (d) measuring the detectable signal;
- (e) isolating or identifying as an activator compound a compound that increases said detectable signal 2-fold or higher than normal and/or isolating or identifying as an inhibitor compound a compound that decreases said detectable signal half or less than normal; and (f) optimizing the isolated or identified compound as a pharmaceutical composition.
- (15) A kit for screening a compound in respect of activity to inhibit or promote NF-  $\kappa$  B activation, which comprises:
- (a) a cell comprising a gene encoding a protein that activates NF-  $\kappa$  B, and a component that provides a detectable signal upon activation of NF-  $\kappa$  B; and
- (b) reagents for measuring the detectable signal.
- (16) A monoclonal or polyclonal antibody that specifically binds to the protein according to above item (1), (2) or (7).
- (17) A process for producing a monoclonal or polyclonal antibody according to above item that specifically binds to the protein of above item (1),(2) or (7), which comprises administering the protein according to above item (1), (2) or (7) as an antigen or epitope-bearing fragments to a non-human animal.
- (18) An antisense oligonucleotide complementary to the polynucleotide according to any one of above items (3) to (6), which prevents NF-  $\kappa$  B activator protein expression.
- (19) A ribozyme which inhibits NF-  $\kappa$  B activation by cleavage of RNA that encodes the protein of above item (1), (2) or (7), or by cleavage of RNA that encodes some protein of the pathway that leads to I  $\kappa$  B degradation.

- (20) A method for treating a disease, which comprises administering to a subject an amount of a compound screened by the process according to above item (13), and/or a monoclonal or polyclonal antibody according to above item (16), and/or an antisense oligonucleotide according to above item (18), and/or a ribozyme according to above item (19) effective to treat a disease selected from the group consisting of inflammation, autoimmune diseases, infectious disease and cancers.
- (21) A pharmaceutical composition produced according to the process of item (14) as an inhibitor or promoter of NF-  $\kappa$  B activation.
- (22) A pharmaceutical composition according to item (21) for the treatment of inflammation, autoimmune diseases, cancers and viral infections.
- (23) A method of treating inflammation, autoimmune diseases, cancers and viral infections, which comprises administering a pharmaceutical composition produced according to the process of above item (14) to a patient suffering from NF-  $\kappa$  B activation.
- (24) A pharmaceutical composition according to item (21) for the treatment of GVHD, dermatosis such as toxic epidermal necrolysis, proliferative nephritides such as IgA nephritis, purpuric nephritis and lupus nephritis, and fulminant hepatitis.
- (25) A method of treating GVHD, dermatosis such as toxic epidermal necrolysis, proliferative nephritides such as IgA nephritis, purpuric nephritis and lupus nephritis, and fulminant hepatitis, which comprises administering a pharmaceutical composition produced according to the process of above item (14) to a patient suffering from inhibition of NF-  $\kappa$  B.
- (26) A pharmaceutical composition which comprises a monoclonal or polyclonal antibody according to item (16)as an active ingredient.
- (27) A pharmaceutical composition which comprises an antisense oligonucleotide according to item (18) as an active ingredient.
- (28) The pharmaceutical composition according to item (26) or (27), wherein the target disease is selected from the group consisting of inflammation, autoimmune diseases, infectious diseases and cancers.
- (29) A method for obtaining a novel gene having a function,

which comprises at least the following steps:

- (a) constructing a full-length cDNA library by the oligo-capping method;
- (b) cotransfecting the full-length cDNA and a plasmid containing a factor emitting a signal indicative of the presence of a protein having the function into cells; and
- (c) selecting a plasmid emitting the signal.
- (30) A computer-readable medium on which a sequence data set has

been stored, said sequence data set comprising at least one nucleotide sequence selected from the group consisting of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175 and 177, and/or at least one amino acid sequence selected from the group consisting of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 and 178.

- (31) A method for calculating identity to other nucleotide sequences and/or amino acid sequences, which comprises comparing data on a medium according to above item (30) with data of said other nucleotide sequences and/or amino acid sequences.
- (32) An insoluble substrate to which polynucleotide comprising all or part of the nucleotide sequences selected from the group consisting of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88 and 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175 and 177, are fixed.
- (33) An insoluble substrate to which polypeptides comprising all or a part of the amino acid sequences selected from the group consisting of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15,

17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 and 178, are fixed.

At first, in order to further clarify the basic feature of the present invention, the present invention is explained by following how the present invention is completed. In order to obtain a new gene having a function of activating NF-  $\kappa$  B, the following experiments were carried out as shown in the examples. First, using the oligo-capping method, a full-length cDNA was produced from mRNA prepared from normal human lung fibroblasts (purchased from Sanko Junyaku Co., Ltd.), and a full-length cDNA library was constructed in which the cDNA was inserted into the vector pME18S-FL3 (GenBank Accession AB009864). Next, the cDNA library was introduced into E. coli cells, and plasmid Then, the pNK  $\kappa$  B-Luc reporter plasmid preparation was carried out per clone. (STRATAGENE) containing a DNA encoding luciferase under control of a promoter activated by NF- kB and the above full-length cDNA plasmid were cotransfected into 293-EBNA cells (Invitrogen). After 24 or 48 hours of culture, luciferase activity was measured, and the plasmid with significantly increased luciferase activity compared to that of a control experiment (vector pME18S-FL3 is introduced into a cell in place of a full-length cDNA)was selected (the selected plasmid showed a 10-fold or more increase in luciferase activity compared to that of the control experiment), and the entire nucleotide sequence of the cDNA cloned into the plasmid was determined. The protein encoded by the cDNA thus obtained shows that this protein is a signal transduction molecule involved in NF-  $\kappa$  B activation.

The present invention is described in detail below.

Related to the amino acid sequences of SEQ ID NOs. 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147,

149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 and 178, the present invention provides for a protein that:

- (a) comprises one of the above amino acid sequences;
- (b) is a peptide having one of the above amino acid sequences;
- (c) activates NF-  $\kappa$  B and consists of an amino acid sequence having at least one amino acid deletion, substitution or addition in the above amino acid sequences;
- (d) comprises an amino acid sequence, which has at least 95% identity, preferably at least 97-99% identity, to an amino acid sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 or 178, over the entire length thereof.

"Identity" as known in the art, is a relationship between two or more protein sequence or two or more polynucleotide sequences, as determined by comparing the sequences. In the art, "identity" also means the degree of sequence relatedness between protein or polynucleotide sequences, as determined by the match between protein or polynucleotide sequences, as the case may be, as determined by the match between strings of such sequences. "Identity" and "similarity" can be readily calculated by known methods. Preferred methods to determine identity are designed to give the largest match between the sequences tested. Methods to determine identity and similarity are codified in publicly available computer programs. "Identity" can be determined by using the BLAST program (for example, Altschul SF, Gish W, Miller W, Myers EW, Lipman DJ., J. Mol. Biol., 215: p403-410 (1990), Altschul SF, Madden TL, Schaffer AA, Zhang Z, Miller W, Lipman DJ., Nucleic Acids Res. 25: p3389-3402 (1997))

The Examples described below demonstrate that the protein consisting of an amino acid sequence of the above SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121,

123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 or 178, is capable of activating NF-  $\kappa$  B.

Related to the polynucleotide sequences of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175 and 177, the present invention further provides an isolated polynucleotide that:

- (a) comprises a nucleotide sequence, which has at least 95% identity, preferably at least 97-99% identity to one of the above sequences;
- (b) is a polynucleotide of one of the above sequences; or
- (c) has a nucleotide sequence encoding a protein which has at least 95% identity, preferably, at least 97-99% identity, to the amino acid sequence of SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 or 178.

Polynucleotides which are identical or almost identical to nucleotide sequences contained in the above nucleotide sequences may be used as hybridization probes to isolate full-length cDNA and genomic clones encoding the protein of the present invention, or cDNA or genomic clones of other genes that have a high sequence similarity to the above sequences, or genomic clones, or may be used as primers for nucleic acid amplification reactions. Typically, these nucleotide sequences are 70% identical, preferably 80% identical, more preferably 90% identical, most preferably 95% identical to the above sequences. The probes or primers will generally comprises at least 15 nucleotides, preferably 30 nucleotides and may have 50 nucleotides. Particularly preferred probes will have between 30 and 50 nucleotides. Particularly preferred primers have between 20 and 25 nucleotides.

The polynucleotide of the present invention may be either in the form of a DNA such as cDNA, a genomic DNA obtained by cloning or synthetically produced, or may be in

the form of RNA such as mRNA. The polynucleotide may be single-stranded or double-stranded. The double-stranded polynucleotides may be double-stranded DNA, double-stranded RNA or DNA:RNA hybrid. The single-stranded polynucleotide may be sense strand also known as coding strand or antisense strand also known as non-coding strand.

Those skilled in the art can prepare a protein having the same NF-  $\kappa$  B activating activity as the protein having an amino acid sequence of SEQ ID NO:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 or 178, by means of appropriate substitution of an amino acid in the protein using known methods. One such method involves using conventional mutagenesis procedures for the DNA encoding the protein. Another method is, for example, site-directed mutagenesis (e.g., Mutan-Super Express Km Kit from Takara Shuzo Co., Ltd.). Mutations of amino acids in proteins may also occur in nature. Thus, the present invention also includes a mutated protein which is capable of activating NF-  $\kappa$  B and which has at least one amino acid deletion, substitution or addition relative to the protein of SEO ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 or 178, and the DNA encoding the protein. The number of mutations is preferably up to 10, more preferably up to 5, most preferably up to 3.

The substitutions of amino acids are preferably conservative substitutions, specific examples of which are substitutions within the following groups: (glycine, alanine), (valine, isoleucine, leucine), (aspartic acid, glutamic acid), (asparagine, glutamine), (serine, threonine), (lysine, arginine) and (phenylalanine, tyrosine).

Based on the nucleotide sequences (e.g., SEQ ID NO: 2) encoding a protein

consisting of an amino acid sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 or 178, or a fragment thereof, those skilled in the art can routinely isolate a DNA with a high sequence similarity to these nucleotide sequences by using hybridization techniques and the like, and obtain proteins having the same NF-  $\kappa$  B activating activity as the protein having of an amino acid sequence of SEQ ID NO:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 or 178. Thus, the present invention also includes a protein that activates NF-  $\kappa$  B and comprises an amino acid sequence having a high identity to the amino acid sequence of the above SEQ ID NO:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 or 178. "High identity" refers to an amino acid sequence having an identity of at least 90%, preferably at least 97-99% over the entire length of an amino acid sequence expressed by the above SEQ ID NO:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 or 178.

The proteins of the present invention may be natural proteins derived from any human or animal cells or tissues, chemically synthesized proteins, or proteins obtained by genetic recombination techniques. The protein may or may not be subjected to post-translational modifications such as sugar chain addition or phosphorylation.

The present invention also includes a polynucleotide encoding the above protein of the present invention. Examples of nucleotide sequences encoding a protein consisting of an amino acid sequence of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 and 178 include nucleotide sequences of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175 and 177. The DNA includes cDNA, genomic DNA, and chemically synthesized DNA. In accordance with the degeneracy of the genetic code, at least one nucleotide in the nucleotide sequence encoding a protein consisting of an amino acid sequence of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 and 178 can be substituted with other nucleotides without altering the amino acid sequence of the protein produced from the gene. Therefore, the DNA sequences of the present invention also include nucleotide sequences altered by substitution based on the degeneracy of the genetic code. Such DNA sequences can be synthesized using known methods.

The DNA of the present invention includes a DNA which encodes a protein capable of activating NF-  $\kappa$  B and hybridizes under stringent conditions with the DNA sequence of the above nucleotide sequence of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150,

151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175 or 177. Stringent conditions are apparent to those skilled in the art, and can be easily attained in accordance with various laboratory manuals such as T. Maniatis et al., Molecular Cloning A Laboratory Manual, Cold Spring Harbor Laboratory 1982, 1989.

That is, "stringent conditions" refer to overnight incubation at  $37^{\circ}$ C in a hybridization solution containing 30% formamide,  $5 \times SSC$  (0.75 M NaCl, 75mM trisodium citrate),  $5 \times Denhardt's$  solution, 0.5% SDS,  $100 \mu$  g/ml denatured, sheared salmon sperm DNA) followed by washing (three times) in  $2 \times SSC$ , 0.1% SDS for 10 minutes at room temperature, then followed by washing (two times) in 0.2 x SSC, 0.1% SDS for 10 minutes at  $37^{\circ}$ C (low stringency). Preferred stringent conditions are overnight incubation at  $42^{\circ}$ C in a hybridization solution containing 40% formamide, followed by washing (three times) in  $2 \times SSC$ , 0.1% SDS for 10 minutes at room temperature, then followed by washing (two times) in 0.2 x SSC, 0.1% SDS for 10 minutes at  $42^{\circ}$ C (moderate stringency). More preferred stringent conditions are overnight incubation at  $42^{\circ}$ C in a hybridization solution containing 50% formamide, followed by washing (three times) in  $2 \times SSC$ , 0.1% SDS for 10 minutes at room temperature, followed by washing (two times) in  $0.2 \times SSC$ , 0.1% SDS for 10 minutes at room temperature, followed by washing (two times) in  $0.2 \times SSC$ , 0.1% SDS for 10 minutes at 70°C (high stringency). The DNA sequence thus obtained must encode a protein capable of activating NF-  $\kappa$  B.

The present invention also includes a polynucleotide comprising a nucleotide sequence which encodes a protein capable of activating NF-  $\kappa$  B and has a high sequence similarity to the nucleotide sequence of the polynucleotide according to above item (3) or (4). Typically these nucleotide sequence are 95% identical, preferably 97% identical, more preferably 98-99% identical, most preferably at least 99% identical to the nucleotide sequence of the polynucleotide according to above item (3) or (4) over the entire length thereof.

The above nucleotide sequence of the present invention can be used to produce the above protein using recombinant DNA techniques. In general, the DNA and peptide of the present invention can be obtained by:

(A) cloning the DNA encoding the protein of the present invention;

- (B) inserting the DNA encoding the entire coding region of the protein or a part thereof into an expression vector to construct a recombinant vector;
- (C) transforming host cells with the recombinant vector thus constructed; and
- (D) culturing the obtained cells to express the protein or its analogue, and then purifying it by column chromatography.

General procedures necessary to handle DNA and recombinant host cells (e.g., E. coli) in the above steps are well known to those skilled in the art, and can be easily carried out in accordance with various laboratory manuals such as T. Maniatis et al., supra. All the enzymes, reagents, etc., used in these procedures are commercially available, and unless otherwise stated, such commercially available products can be used according to the use conditions specified by the manufacturer's instructions to attain completely its objects. The above steps (A) to (D) can be further illustrated in more details as follows.

Techniques for cloning the DNA encoding the protein of the present invention include, in addition to the methods described in the specification of the present application, PCR amplification using a synthetic DNA having a part of the nucleotide sequence of the present invention (e.g., SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175 or 177) as a primer, and selection of the DNA inserted into a suitable vector by hybridization with a labeled DNA fragment encoding a partial or full coding region of the protein of the present invention or a labeled synthetic Another technique involves direct amplification from total RNAs or mRNA DNA. fractions prepared from cells or tissues, using the reverse transcriptase polymerase chain reaction (RT-PCR method). As a DNA inserted into a suitable vector, for example, a commercially available library (e.g., from CLONTECH and STRATAGENE) can be used. Techniques for hybridization are normally used in the art, and can be easily carried out in accordance with various laboratory manuals such as T. Maniatis et al., supra. Depending on the intended purpose, the cloned DNA encoding the protein of the present invention can

be used as such or if desired after digestion with a restriction enzyme or addition of a linker. The DNA thus obtained may have a nucleotide sequence of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175 or 177, or a polynucleotide of above items (3) to (6). The DNA sequence to be inserted into an expression vector in the above step (B) may be a full-length cDNA or a DNA fragment encoding the above full-length protein, or a DNA fragment constructed so that it expresses a part thereof.

Thus, the present invention also includes a recombinant vector, which comprises the above DNA sequence. The expression vector for the protein of the present invention can be produced, for example, by excising the desired DNA fragment from the DNA encoding the protein of the present invention, and ligating the DNA fragment downstream of a promoter in a suitable expression vector.

Expression vectors for use in the present invention may be any vectors derived from prokaryotes (e.g., E. coli), yeast, fungi, insect viruses and vertebrate viruses so long as such vectors are replicable. However, the vectors should be selected to be compatible with microorganisms or cells used as hosts. Suitable combinations of host cell – expression vector systems are selected depending on the desired expression product.

When microorganisms are used as hosts, plasmid vectors compatible with these microorganisms are generally used as replicable expression vectors for recombinant DNA molecules.

For example, the plasmids pBR322 and pBR327 can be used to transform E. coli. Plasmid vectors normally contain an origin of replication, a promoter, and a marker gene conferring upon a recombinant DNA a phenotype useful for selecting the cells transformed with the recombinant DNA. Example of such promoters include a  $\beta$ -lactamase promoter, lactose promoter and tryptophan promoter. Examples of such marker genes include an ampicillin resistance gene, and a tetracycline resistance gene. Examples of suitable

expression vectors include the plasmids pUC18 and pUC19 in addition to pBR322, pBR327.

In order to express the DNA of the present invention in yeast, for example, YEp24 can be used as a replicable vector. The plasmid YEp24 contains the URA3 gene, which can be employed as a marker gene. Examples of promoters in expression vectors for yeast cells include promoters derived from genes for 3-phosphoglycerate kinase, glyceraldehyde-3-phosphate dehydrogenase and alcohol dehydrogenase.

Examples of promoters and terminators for use in expression vectors to express the DNA of the present invention in fungal cells include promoters and terminators derived from genes for phosphoglycerate kinase (PGK), glyceraldehyde-3-phosphate dehydrogenase (GAPD) and actin. Examples of suitable expression vectors include the plasmids pPGACY2 and pBSFAHY83.

Examples of promoters for use in expression vectors to express the DNA of the present invention in insect cells include a polyhedrin promoter and P10 promoter.

Recombinant vectors used to express the DNA of the present invention in animal cells normally contain functional sequences to regulate genes, such as an origin of replication, a promoter to be placed upstream of the DNA of the present invention, a ribosome-binding site, a polyadenylation site and a transcription termination sequence. Such functional sequences, which can be used to express the DNA of the present invention in eukaryotic cells, can be obtained from viruses and viral substances. Examples of such functional sequences include an SR  $\alpha$  promoter, SV40 promoter, LTR promoter, CMV (cytomegalovirus) promoter and HSV-TK promoter. Among them, a CMV promoter and SR  $\alpha$  promoter can be preferably used. As promoters to be placed inherently upstream of the gene encoding the protein of the present invention, any promoters can be used so long as they are suitable for use in the above host-vector systems. Examples of origins of replication include foreign origins of replication, for example, those derived from viruses such as adenovirus, polyoma virus and SV40 virus. When vectors capable of integration into host chromosomes are used as expression vectors, origins of replication of the host chromosomes may be employed. Examples of suitable expression vectors include the

plasmids pSV-dhfr (ATCC 37146), pBPV-1(9-1) (ATCC 37111), pcDNA3.1 (INVITROGEN) and pME18S-FL3.

The present invention also includes a transformed cell, which comprises the above recombinant vector.

Microorganisms or cells transformed with the replicable recombinant vector of the present invention can be selected from remaining untransformed parent cells based on at least one phenotype conferred by the recombinant vector. Phenotypes can be conferred by inserting at least one marker gene into the recombinant vector. Marker genes naturally contained in replicable vectors can be employed. Examples of marker genes include drug resistance genes such as neomycin resistance genes, and genes encoding dihydrofolate reductase.

As hosts for use in the above step (C), any of prokaryotes (e.g., E. coli), microorganisms (e.g., yeast and fungi) as well as insect and animal cells can be used so long as such hosts are compatible with the expression vectors used. Examples of such microorganisms include Escherichia coli strains such as E. coli K12 strain 294 (ATCC 31446), E. coli X1776 (ATCC 31537), E. coli C600, E. coli JM109 and E. coli B strain; bacterial strains belonging to the genus Bacillus such as Bacillus subtilis; intestinal bacteria other than E. coli, such as Salmonella typhimurium or Serratia marcescens; and various strains belonging to the genus Pseudomonas. Examples of such yeast include Saccharomyces cerevisiae, Schizosaccharomyces pombe, and Pichia pastoris. Examples of such fungi include Aspergillus nidulans, and Acremonium chrysogenum (ATCC 11550).

As insect cells, for example, Spodoptera frugiperda (Sf cells), High Five TM cells derived from eggs of Trichoplusiani, etc., can be used when the virus is AcNPV. Examples of such animal cells include HEK 293 cells, COS-1 cells, COS-7 cells, Hela cells, and Chinese hamster ovary (CHO) cells. Among them, CHO cells and HEK 293 cells are preferred.

When cells are used as hosts, combinations of expression vectors and host cells to be used vary with experimental objects. According to such combinations, two types of expression (i.e. transient expression and constitutive expression) can be included.

"Transformation" of microorganisms and cells in the above step (C) refers to introducing DNA into microorganisms or cells by forcible methods or phagocytosis of cells and then transiently or constitutively expressing the trait of the DNA in a plasmid or an intra-chromosome integrated form. Those skilled in the art can carry out transformation by known methods [see e.g., "Idenshi Kougaku Handbook (Genetic Engineering Handbook)", an extra issue of "Jikken Igaku (Experimental Medicine)", YODOSHA CO., LTD.]. For example, in the case of animal cells, DNA can be introduced into cells by known methods such as DEAE-dextran method, calcium-phosphate-mediated transfection, electroporation, lipofection, etc. For stable expression of the protein of the present invention using animal cells, there is a method in which selection can be carried out by clonal selection of the animal cells containing the chromosomes into which the introduced expression vectors have been integrated. For example, transformants can be selected using the above selectable marker as an indication of successful transformation. In addition, the animal cells thus obtained using the selectable marker can be subjected to repeated clonal selection to obtain stable animal cell strains highly capable of expressing the protein of the present invention. When a dihydrofolate reductase (DHFR) gene is used as a selectable marker, one can culture animal cells while gradually increasing the concentration of methotrexate (MTX) and select the resistant strains, thereby amplifying the DNA encoding the protein of the present invention together with the DHFR gene to obtain animal cell strains having higher levels of expression.

The above transformed cells can be cultured under conditions which permit the expression of the DNA encoding the protein of the present invention to produce and accumulate the protein of the present invention. In this manner, the protein of the present invention can be produced. Thus, the present invention also includes a process for producing a protein, which comprises culturing a transformed cell comprising the isolated polynucleotide according to above item (3) to (6) under conditions providing expression of the encoded protein and recovering the protein from the culture.

The above transformed cells can be cultured by methods known to those skilled in the art (see e.g., "Bio Manual Series 4", YODOSHA CO., LTD.). For example, animal

cells can be cultured by various known animal cell culture methods including attachment culture such as Petri dish culture, multitray type culture and module culture, attachment culture in which cells are attached to cell culture carriers (microcarriers), suspension culture in which productive cells themselves are suspended. Examples of media for use in the culture include media commonly used for animal cell culture, such as D-MEM and RPMI 1640.

In order to separate and purify the protein of the present invention from the above culture, suitable combinations of per se known separation and purification methods can be Examples such methods include methods based on solubility, such as salting-out and solvent precipitation; methods based on the difference in charges, such as ion-exchange chromatography; methods mainly based on the difference in molecular weights, such as dialysis, ultrafiltration, gel filtration and SDS-polyacrylamide gel electrophoresis; methods based on specific affinity, such as affinity chromatography; methods based on the difference in hydrophobicity, such as reverse phase high performance liquid chromatography; and methods based on the difference in isoelectric points, such as isoelectric focusing. For example, a protein of the present invention can be recovered and purified from recombinant cell cultures by well-known methods including ammonium sulfate or ethanol precipitation, acid extraction, anion cation or exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxyapatite chromatography and lectin chromatography. Most preferably, high performance liquid chromatography is employed for purification. Well known techniques for refolding proteins may be employed to regenerate active conformation when the polypeptide is denatured during intracellular synthesis, isolation or purification.

The protein of the present invention can also be produced as a fusion protein with another protein. These fusion proteins are also included within the present invention. For the expression of such fusion proteins, any vectors can be used so long as the DNA encoding the protein can be inserted into the vectors and the vectors can express the fusion protein. Examples of proteins to which a polypeptide of the present invention can be fused include glutathione S-transferase (GST) and a hexa-histidine sequence (6 x His). The

fusion protein of the protein of the present invention with another protein can be advantageously purified by affinity chromatography using a substance with an affinity for the fusion partner protein. For example, fusion proteins with GST can be purified by affinity chromatography using glutathione as a ligand.

The present invention also includes an inhibitory protein, i.e., a protein capable of inhibiting the activity of the protein of above item (7). Examples of such inhibitory proteins include antibodies, or other proteins that bind to active sites of a protein of the above item (7), thereby inhibiting the expression of their activity.

The present invention also relates to an antibody that specifically binds the protein of the present invention or a fragment thereof, and to production of such an antibody. The antibody is not specifically limited so long as it can recognize the protein of the present Examples of such antibodies include polyclonal antibodies, monoclonal invention. antibodies and their fragments, single chain antibodies and humanized antibodies. Antibody fragments can be produced by known techniques. Examples of such antibody fragments include, but not limited to, F(ab')2 fragments, Fab' fragments, Fab fragments and Fv fragments. The antibody that specifically binds the protein of the present invention can be produced using the protein of the present invention or a peptide thereof as an immunogen according to per se known process for producing antibodies or antisera. For example, a monoclonal or polyclonal antibody can be produced by administering the protein according to above item (1) or (2) as an antigen or epitope-bearing fragments to a non-human animal. Such methods are described, for example, in "Shin Idenshi Kougaku Handbook (New Genetic Engineering Handbook)", the third edition, an extra issue of "Jikken Igaku (Experimental Medicine)", YODOSHA CO., LTD.

In the case of polyclonal antibodies, for example, the protein of the present invention or a peptide thereof can be injected to animals such as rabbits to produce antibodies directed against the protein or peptide, and then their blood can be collected. The polyclonal antibodies can be purified from the blood, for example, by ammonium sulfate precipitation or ion-exchange chromatography, or by using the affinity column on which the protein has been immobilized.

In the case of monoclonal antibodies, for example, animals such as mice are immunized with the protein of the present invention, their spleen is removed and homogenized to obtain spleen cells, which are then fused with mouse myeloma cells by using a reagent such as polyethylene glycol. From the resulting hybrid cells (i.e. hybridoma cells), the clone producing the antibody directed against the protein of the present invention can be selected. Then, the resulting clonal hybridoma cells can be implanted intraperitoneally into mice, the ascitic fluid recovered from the mice. The resulting monoclonal antibody can be purified, for example, by ammonium sulfate precipitation or ion-exchange chromatography, or by using the affinity column on which the protein has been immobilized.

When the resulting antibody is used to administer it to humans, it is preferably used as a humanized antibody or human antibody in order to reduce its immunogenicity. The humanized antibody can be produced using transgenic mice or other mammals. For a general review of these humanized antibodies and human antibodies, see, for example, Morrison, S.L. et al., Proc. Natl. Acad. Sci. USA, 81:6851-6855 (1984); Jones, P.T. et al., Nature 321:522-525 (1986); Hiroshi Noguchi, Igaku no Ayumi (J. Clin. Exp. Med.) 167:457-462 (1993); Takashi Matsumoto, Kagaku to Seibutsu (Chemistry and Biology) 36:448-456 (1998). Humanized chimeric antibodies can be produced by linking a V region of a mouse antibody to a C region of a human antibody. Humanized antibodies can be produced by substituting a sequence derived from a human antibody for a region other than a complementarity-determining region from a mouse monoclonal antibody. addition, human antibodies can be directly produced in the same manner as the production of conventional monoclonal antibodies by immunizing the mice whose immune systems have been replaced with human immune systems. These antibodies can be used to isolate or to identify clones expressing the protein or to purify the protein of the present invention from a cell extract or transformed cells producing the protein of the present invention. These proteins can also be used to construct ELISA, RIA (radioimmunoassay) and western blotting systems. These assay systems can be used for diagnostic purposes for detecting an amount of the protein of the present invention present in a body sample in a tissue or a fluid

in the blood of an animal, preferably human. For example, they can be used for diagnosis of a disease characterized by undesirable activation of HF-  $\kappa$  B resulting from (expression) abnormality of the protein of the present invention, such as inflammation, autoimmune disease, infection (for example, HIV infection), cancer and the like. In order to provide a basis for diagnosis of a disease, a standard value must be established. However, this is a well-known technique to those skilled in the art. For example, a method of calculating the standard value comprises binding a body fluid or a cell extract of normal individual of a human or an animal to an antibody against the protein of the present invention under a suitable condition for the complex formation, detecting the amount of the antibody-protein complex by chemical or physical means and then calculating the standard value for the normal sample using a standard curve prepared from a standard solution containing a known amount of an antigen (the protein of the present invention). The presence of a disease can be confirmed by deviation from the standard value obtained by comparison of the standard value with the value obtained from a sample of an individual latently suffering from a disease associated with the protein of the present invention. These antibodies can also be used as reagents for studying functions of the protein of the present invention.

The antibodies of the present invention can be purified and then administered to patients characterized by undesirable activation of HF-  $\kappa$  B resulting from (expression) abnormality of the protein of the present invention, such as inflammation, autoimmune disease, infection (such as HIV infection), cancer and the like. Thus in another aspect, the present invention is a pharmaceutical composition which comprises the above antibody as an active ingredient, and therapy using the antibody of the present invention. In such pharmaceutical compositions, the active ingredient may be combined with other therapeutically ingredients active or inactive ingredients (e.g., conventional pharmaceutically acceptable carriers or diluents such as immunogenic adjuvants) and physiologically non-toxic stabilizers and excipients. The resulting combinations can be sterilized by filtration, and formulated into vials after lyophilization or into various dosage forms in stabilized and preservable aqueous preparations. Administration to a patient can be

intra-arterial administration, intravenous administration and subcutaneous administration, which are well known to those skilled in the art. The dosage range depends upon the weight and age of the patient, route of administration and the like. Suitable dosages can be determined by those skilled in the art. These antibodies exhibit therapeutic activity by inhibiting the NF-  $\kappa$  B activation mediated by the protein of the present invention.

The DNA of the present invention can also be used to isolate, identify and clone other proteins involved in intracellular signal transduction processes. For example, the DNA sequence encoding the protein of the present invention can be used as a "bait" in yeast two-hybrid systems (see e.g., Nature 340:245-246 (1989)) to isolate and clone the sequence encoding a protein ("prey") which can associate with the protein of the present invention. In a similar manner, it can be determined whether the protein of the present invention can associate with other cellular proteins (e.g., NIK and TRAF2). In another method, proteins which can associate with the protein of the present invention can be isolated from cell extracts by immunoprecipitation [see e.g., "Shin Idenshi Kougaku Handbook (New Genetic Engineering Handbook)", an extra issue of "Jikken Igaku (Experimental Medicine)", YODOSHA CO., LTD.] using antibodies directed against the protein of the present invention. In still another method, the protein of the present invention can be expressed as a fusion protein with another protein as described above, and immunoprecipitated with an antibody directed against the fusion protein in order to isolate a protein which can associate with the protein of the present invention.

The diagnostic assays offer a process for diagnosing diseases or determining a susceptibility to the diseases through detection of mutation in a gene for a protein according to item (1), (2) or (7) which has a function of activating NF-  $\kappa$  B, by the methods described. In addition, such diseases may be diagnosised by methods comprising determining from a sample derived from a subject an abonormally decreased or increased level of protein or mRNA. Decreased or increased expression can be measured at the RNA level using any of the methods well known in the art for the quantitation of polynucleotides, for example, nucleic acid amplification methods such as RT-PCR, and methods such as RNase protection assay, Northern blotting and other hybridization methods. Assay techniques that can be used

to determine levels of a protein in a sample derived from a host are well-known to those skilled in the art. Such assay methods include radioimmunoassays, competitive-binding assays, Western blot analysis and ELISA assays. The DNA of the present invention can be used to detect abnormality in the DNA or mRNA encoding the protein of the present invention or a peptide fragment thereof. The invention relates to a method for diagnosing a disease, or susceptibility to a disease associated with the expression of the protein according to above item (1), (2) or (7) in a subject, which comprises determining mutations in the polynucleotide sequence encoding the protein. Thus, for example, the DNA of the present invention is useful for gene diagnosis regarding damage, mutations, and reduced, increased or over- expression of the DNA or mRNA. That is, the present invention includes a method for diagnosing a disease associated with the expression or activity of NF- $\kappa$  B in a subject, which comprises the steps of:

A process for diagnosing a disease or susceptibility to a disease in a subject related to espression or activity of the protein of above item (1) or (2) in a subject comprising:

- (a) determining the presence or absence of a mutation in the nucleotide sequence encoding said protein in the genome of said subject, and/or
- (b) analyzing the amount of expression of said protein in a sample derived from said subject,

wherein a diagnosis of disease is made when the amount of the protein expressed is 2-fold or higher than normal, or half or lower than normal.

When the nucleotide sequence encoding the protein of above item (1), (2) or (7) which has a function of activating NF-  $\kappa$  B, contains a mutation according to the above step (a), the mutation may cause a disease associated with NF-  $\kappa$  B activation. When the amount of the expression of the protein of above item (1), (2) or (7) is different from the normal value according to the above step (b), the abnormal expression of the novel protein of the present invention which acts to activate NF-  $\kappa$  B may be responsible for diseases associated with NF-  $\kappa$  B activation. In the above step (a), determination of the presence or absence of a mutation in the nucleotide sequence encoding the protein of above item (1),(2) or (7) which has a function of activating NF-  $\kappa$  B, may involve RT-PCR using a part of the

nucleotide sequences of genes encoding these proteins as a primer, followed by conventional DNA sequencing to detect the presence or absence of the mutation. PCR-SSCP [Genomics 5:874-879 (1989); "Shin Idenshi Kougaku Handbook (New Genetic Engineering Handbook)", an extra issue of "Jikken Igaku (Experimental Medicine)", YODOSHA CO., LTD.] can also be used to determine the presence or absence of the mutation.

Measurement of the amount of the expression of the protein in the above step (b) may involve, for example, using the antibody of above item (16). Sequencing the nucleotide sequence may involve, for example, RT-PCR using a part of the nucleotide sequence of the gene of above items (3) to (6) as a primer, followed by conventional DNA sequencing to detect the presence or absence of the mutation. PCR-SSCP [Genomics 5:874-879 (1989); "Shin Idenshi Kougaku Handbook (New Genetic Engineering Handbook)", an extra issue of "Jikken Igaku (Experimental Medicine)", YODOSHA CO., LTD.] can also be used to determine the presence or absence of the mutation.

The present invention also relates to a method for screening compounds which inhibit or promote NF-  $\kappa$  B activation using the proteins of the invention, which comprises the steps of:

- (a) providing a cell with a gene encoding a protein that activates NF-  $\kappa$  B, and a component that provides a detectable signal upon activation of NF-  $\kappa$  B:
- (b) culturing the transformed cell under conditions, which permit the expression of the gene in the transformed cell;
- (c) contacting the transformed cell with one or more compounds; and
- (d) measuring the detectable signal; and
- (e) isolating or identifying as an activator compound a compound that increases said detectable signal 2-fold or higher than normal and isolating or identifying as an inhibitor compound a compound that decreases said detectable signal half or higher than normal.

Examples of components capable of providing a detectable signal include reporter genes. Reporter genes are used instead of directly detecting the activation of transcription factors of interest. The transcriptional activity of a promoter of a gene is analyzed by

linking the promoter to a reporter gene and measuring the activity of the product of the reporter gene ("Bio Manual Series 4" (1994), YODOSHA CO., LTD.).

Any peptide or protein can be used so long as those skilled in the art can measure the activity or amount of the expression product (including the amount of the produced mRNA) of the reporter genes. For example, enzymatic activity of chloramphenicol acetyltransferase,  $\beta$  -galactosidase, luciferase, etc., can be measured. Any reporter plasmids can be used to evaluate NF-  $\kappa$  B activation so long as the reporter plasmids have an NF-  $\kappa$  B recognition sequence inserted upstream of the reporter gene. For example, pNF-  $\kappa$  B-Luc (STRATAGEGE) can be used. Other examples include NF-  $\kappa$  B dependent reporter plasmids described in Tanaka S. et al., J. Vet. Med. Sci. Vol.59 (7); Rothe M. et al., Science Vol.269, p.1424-1427 (1995).

Any host cells may be used so long as NF-  $\kappa$  B activation can be detected in the host cells. Preferred host cells are mammalian cells such as 293-EBNA cells. Transformation and culture of the cells can be carried out as described above.

In a specific embodiment, the method for screening a compound which inhibits or promotes NF-  $\kappa$  B activation comprises culturing the transformed cell for a certain period of time, adding a certain amount of a test compound, measuring the reporter activity expressed by the cell after a certain period of time, and comparing the activity with that of a cell to which the test compound has not been added. The reporter activity can be measured by methods known in the art (see e.g., "Bio Manual Series 4" (1994), YODOSHA CO., LTD.). Examples of test compounds include, but not limited to, low molecular weight compounds and peptides. Test compounds may be artificially synthesized compounds or naturally occurring compounds. Test compounds may be a single compound or mixtures. Examples of such detectable signals which may be measured include the amount of mRNA or proteins for genes whose expression is known to be induced by NF-  $\kappa$  B activation (e.g., genes for IL-1 and TNF-  $\alpha$  ) in addition to the above reporter genes. The amount of mRNA can be measured, for example, by northern hybridization, RT-PCR, etc. The amount of proteins can be measured, for example, by using antibodies. The antibodies may be produced by known methods. Commercially available antibodies(from, e.g., Wako Pure

Chemical Industries, Ltd.) can also be used.

It is also possible to produce a pharmaceutical composition according to the following steps (a) to (f):

- (a) providing a cell with a gene encoding a protein that activates NF-  $\kappa$  B, and a component that provides a detectable signal upon activation of NF-  $\kappa$  B;
- (b) culturing the transformed cell under conditions, which permit the expression of the gene in the transformed cell;
- (c) contacting the transformed cell with one or more candidate compounds;
- (d) measuring the detectable signal;
- (e) isolating or identifying as an activator compound a compound that increases said detectable signal 2-fold or higher than normal and isolating or identifying as an inhibitor compound a compound that decreases said detectable signal half or less than normal; and (f) optimizing the isolated or identified compound as a pharmaceutical composition.

The protein of the present invention may also be used in a method for the structure-based design of an agonist, antagonist or inhibitor of the protein, by:

- (a) determining in the first instance the three-dimensional structure of the protein;
- (b) deducing the three-dimensional structure for the likely reactive or binding site(s) of an agonist, antagonist or inhibitor;
- (c) synthesising candidate compounds that are predicted to bind to or react with the deduced binding or reactive site; and
- (d) testing whether the candidate compounds are indeed agonists, antagonists or inhibitor.

The present invention also includes a compound obtainable by the above screening method. However, the screening method of the present invention is not limited to the above method. The present invention also includes a process for producing the pharmaceutical composition by the method of above item (14).

There is no special limitation to the above candidate compounds. Such compounds include low molecular weight compounds and peptides. They may be artificially synthesised compounds and naturally occurring compounds. As the compounds obtained by the above screening methods have a function of inhibiting or promoting NF-  $\kappa$  B

activation, they are useful as therapeutic or preventive pharmaceuticals for the treament of diseases resulting from unfavorable activation or inactivation of NF-  $\kappa$  B. In order to isolate and purify the target compounds from the mixture, it is suitable to combine the known methods such filtration, extraction, washings, drying, concentration. crystallization, various chromatography. When obtainment of a salt of the compounds is desired, a compound which is obtained in the form of a salt can be purified as it is. A compound which is obtained in the free form can be converted into a salt by isolating and purifying a salt obtained by dispersing or dissolving the compound into a suitable solvent and then adding a desired acid or base. When the compounds or salts thereof obtained by the method of the present invention are used as a pharmceutical composition, they can be formulated. The above compounds or their pharmaceutically acceptable salts in an amount effective as an active ingredient, and pharmaceutically acceptable carriers can be mixed. A form of formulation suitable for the mode of administration is selected. A composition suitable for oral administration includes a solid form such as tablet, granule, capsule, pill and powder, and solution form such as solution, syrup, elixir and dispersion.A form useful for parenteral administration includes sterile solution, dispersion, emulsion and suspension. The above carriers include, for example, sugars such as gelatin, lactose and glucose, starches such as corn, wheat, rice and maize, fatty acids such as stearic acid, salts of fatty acids such as calcium stearate, magnesium stearate, talc, vegetable oil, alcohol such as stearyl alcohol and benzyl alcohol, gum, and polyalkylene glycol. Examples of such liquid carriers include generally water, saline, sugar solution of dextrose and the lile, glycols such as ethylene glycol, propylene glycol and polyethylene glycol.

The present invention also includes a kit for screening compounds for activity as an inhibitor or promoter of NF-  $\kappa$  B activation. The kit comprises reagents and the like necessary for screening compounds for inhibiting or promoting activity for NF-  $\kappa$  B activation, including:

(a) a cell comprising a gene encoding a protein that activates NF-  $\kappa$  B, and a component that provides a detectable signal enabling detection of NF-  $\kappa$  B activation after activation of NF-  $\kappa$  B; and

(b) reagents for measuring the detectable signal.

In another aspect, the present invention relates to a diagnostic kit which comprises:

(a) a polynucleotide of the present invention having a nucleotide sequence expressed by SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62; 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175 or 177;

- (b) a nucleotide sequence complementary to that of (a);
- (c) a protein of the present invention having an amino acid sequence expressed by SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, or 178, or a fragment thereof; or
- (d) an antibody to the protein of the present invention of (c).

A kit comprising at least one of (a) to (d) is useful for diagnosing a disease or susceptibility to a disease such as inflammation, autoimmune diseases, infectious diseases (e.g., HIV infection) and cancers.

Because NF-  $\kappa$  B is involved in a wide variety of pathological conditions such as inflammation, autoimmune diseases, cancers and viral infections, it is an attractive target for drug design and therapeutic intervention. Many experiments show that the inhibition of NF-  $\kappa$  B activity may have significant physiological effects [see e.g., Ann. Rheum. Ds. 57:738-741 (1998); American Journal of Pathology 152:793-803 (1998); ARTHRITIS & RHEUMATISM 40:226-236 (1997); Am. J. Respir. Crit. Care Med. 158:1585-1592 (1998); J. Exp. Med. 188:1739-1750 (1998); Gut 42:477-484 (1998); The Journal of Immunology 161:4572-4582 (1998); Nature Medicine 3:894-899 (1997)]. The finding of the new protein described herein capable of activating NF-  $\kappa$  B has provided a new method for inhibiting an abnormal NF-  $\kappa$  B function. Thus, the present invention also relates to use of

a compound which inhibits the function of the protein capable of activating NF-  $\kappa$  B described above, for inhibiting NF-  $\kappa$  B activation. The compound obtained by the above screening method, which inhibits NF-  $\kappa$  B activation, is useful as a medicament to treat or prevent diseases characterized by undesirable activation of NF-  $\kappa$  B, such as inflammation, autoimmune diseases, infectious diseases (e.g., HIV infection) and cancers. Recently, it has also become apparent that NF-  $\kappa$  B activation inhibits apoptosis of cells. The compound obtained by the above screening method, which inhibits NF-  $\kappa$  B activation, may be capable of stimulating apoptosis. Diseases which may be treated by the induction of apoptosis include tumors.

On the other hand, diseases which may be treated by the inhibition of apoptosis include GVHD, skin diseases such as toxic epidermal necrolysis (TEN), proliferative nephritides (e.g., IgA nephritis, purpuric nephritis and lupus nephritis) and fulminant hepatitis. Thus, the compound obtained by the above screening method, which promotes NF-  $\kappa$  B activation, is useful as a medicament to treat or prevent these diseases.

In addition, the gene encoding the protein of the present invention is useful for gene therapy to treat various diseases such as cancers, autoimmune diseases, allergy diseases and inflammatory response. "Gene therapy" refers to administering into the human body a gene or a cell into which a gene has been introduced. The protein of the present invention and the DNA encoding the protein can also be used for diagnostic purposes.

The compound obtained by the screening method of the present invention or a salt thereof can be formulated into the above pharmaceutical compositions (e.g., tablets, capsules, elixirs, microcapsules, sterile solutions and suspensions) according to conventional procedures. The formulations thus obtained are safe and of low toxicity, and can be administered, for example, to humans and mammals (e.g., rats, rabbits, sheep, pigs, cattle, cats, dogs and monkeys). Administration to patients can be carried out by methods known in the art, such as intra-arterial injection, intravenous injection and subcutaneous injection. The dosage may vary with the weight and age of the patient as well as a mode of administration, but those skilled in the art can appropriately select suitable dosages. When

the compound can be encoded by DNA, the DNA can be inserted into a vector for gene therapy, and gene therapy can be carried out. The dosage and mode of administration may vary with the weight, age and symptoms of the patient, but those skilled in the art can appropriately select them. Thus, the present invention also relates to a pharmaceutical composition which comprises the above compound as an active ingredient.

In addition, the above compound is useful as a medicament to treat or prevent diseases characterized by undesirable activation of NF-  $\kappa$  B, such as inflammation, autoimmune diseases, viral diseases, infectious diseases and cancers. Thus, the present invention also relates to a pharmaceutical composition for inflammation, autoimmune diseases, viral diseases, cancers, etc., which comprises the above compound. Specifically, the pharmaceutical composition is useful as a therapeutic and prophylactic drug against, for example, rheumatoid arthritis, osteoarthritis, systemic lupus erythematosus, diabetes, sepsis, asthma, allergic rhinitis, ischemic heart diseases, inflammatory intestinal diseases, subarachnoid hemorrhage, viral hepatitis and AIDS.

The present invention also relates to the use of a pharmaceutical composition produced according to above item (14) for manufacturing a medicament against inflammation, autoimmune diseases, viral diseases, cancers, etc. The present invention also includes an antisense oligonucleotide against a gene of any one of above items (3) to (6). An antisense oligonucleotide refers to an oligonucleotide complementary to the target gene sequence. The antisense oligonucleotide can inhibit the expression of the target gene by inhibiting RNA functions such as translation to proteins, transport to the cytoplasm and other activity necessary for overall biological functions. In this case, the antisense oligonucleotide may be RNA or DNA. The DNA sequence of the present invention can be used to produce an antisense oligonucleotide capable of hybridizing with the mRNA transcribed from the gene encoding the protein of the present invention. It is known that an antisense oligonucleotide generally has an inhibitory effect on the expression of the corresponding gene (see e.g., Saibou Kougaku Vol.13, No.4 (1994)). The oligonucleotide containing an antisense coding sequence against a gene encoding the protein of the present invention can be introduced into a cell by standard methods. The oligonucleotide

effectively blocks the translation of mRNA of the gene encoding the protein of the present invention, thereby blocking its expression and inhibiting undesirable activity.

The oligonucleotide of the present invention may be a naturally occurring oligonucleotide or its modified form [see e.g., Murakami & Makino, Saibou Kougaku Vol.13, No.4, p.259-266 (1994); Akira Murakami, Tanpakushitsu Kakusan Kouso (PROTEIN, NUCLEIC ACID AND ENZYME) Vol.40, No.10, p.1364-1370 (1995),Tunenari Takeuchi et al., Jikken Igaku (Experimental Medicien) Vol. 14, No. 4 p85-95(1996)]. Thus, the oligonucleotide may have modified sugar moieties or inter-sugar moieties. Examples of such modified forms include phosphothioates and other sulfur-containing species used in the art. According to several preferred embodiments of the present invention, at least one phosphodiester bond in the oligonucleotide is substituted with the structure which can enhance the ability of the composition to permeate cellular regions where RNA with the activity to be regulated is located.

Such substitution preferably involves a phosphorothioate bond, a phosphoramidate bond, methylphosphonate bond, or a short-chain alkyl or cycloalkyl structure. The oligonucleotide may also contain at least some modified base forms. Thus, it may contain purine and pyrimidine derivatives other than naturally occurring purine and pyrimidine. Similarly, the furanosyl moieties of the nucleotide subunits can be modified so long as the essential purpose of the present invention is attained. Examples of such modifications include 2'-O-alkyl and 2'-halogen substituted nucleotides. Examples of modifications in sugar moieties at their 2-position include OH, SH, SCH<sub>3</sub>, OCH<sub>3</sub>, OCN or O(CH<sub>2</sub>)<sub>n</sub>CH<sub>3</sub>, wherein n is 1 to about 10, and other substituents having similar properties. All the analogues are included in the scope of the present invention so long as they can hybridize with the mRNA of the gene of the present invention to inhibit functions of the mRNA.

The oligonucleotide of the present invention contains about 3 to about 50 nucleotides, preferably about 8 to about 25 nucleotides, more preferably about 12 to about 20 nucleotides. The oligonucleotide of the present invention can be produced by the well-known solid phase synthesis technique. Devices for such synthesis are commercially available from some manufactures including Applied Biosystems. Other oligonucleotides

such as phosphothioates can also be produced by methods known in the art.

The oligonucleotide of the present invention is designed to hybridize with the mRNA transcribed from the gene of the present invention. Those skilled in the art can easily design an antisense oligonucleotides based on a given gene sequence (For example, Murakami and Makino: Saibou Kougaku Vol. 13 No.4 p259-266 (1994), Akira Murakami: Tanpakushitsu Kakusan Kouso (PROTEIN, NUCLEIC ACID AND ENZYME) Vol. 40 No.10 p1364-1370 (1995), Tunenari Takeuchi et al., Jikken Igaku (Experimental Medicine) Vol. 14 No. 4 p85-95 (1996)). Recent sutudy suggests that antisense oligonucleotides which are designed in a region containing 5' region of mRNA, preferably,the translation initaiation site, are most effective for the inhibition of the expression of a gene. The length of the antisense oligonucleotides is preferably 15 to 30 nucleotides and more preferably 20 to 25 nucleotides. It is important to confirm no interaction with other mRNA and no formation of secondary structure in the oligonucleotide sequence by homology search. The evaluation of whether the designed antisense oligonucleotide is functional or not can be determined by introducing the antisence oligonucleotide into a suitable cell and measuring the amount of the target mRNA, for example by northern blotting or RT-PCR, or the amount of the target protein, for example by western blotting or fluorescent antibody technique, to confirm the effect of expression inhibition

Another method includes the triple helix technique. This technique involves forming a triple helix on the targeted intra-nuclear DNA sequence, thereby regulating its gene expression, mainly at the transcription stage. The oligonucleotide is designed mainly in the gene region involved in the transcription and inhibits the transcription and the production of the protein of the present invention. Such RNA, DNA and oligonucleotide can be produced using known synthesizers.

The oligonucleotide may be introduced into the cells containing the target nucleic acid sequence by any of DNA transfection methods such as calcium phosphate method, electroporation, lipofection, microinjection, or gene transfer methods including the use of gene transfer vectors such as viruses. An antisense oligonucleotide expression vector can be prepared using a suitable retrovirus vector, then the expression vector can be introduced

into the cells containing the target nucleic acid sequence by contacting the vector with the cells in vivo or ex vivo.

The DNA of the present invention can be used in the antisense RNA/DNA technique or the triple helix technique to inhibit NF-  $\kappa$  B activation mediated by the protein of the present invention.

The antisense oligonucleotide against the gene encoding the protein of the present invention is useful as a medicament to treat or prevent diseases characterized by undesirable activation of NF-  $\kappa$  B, such as inflammation, autoimmune diseases, infectious diseases (e.g., HIV infection) and cancers. Thus, the present invention also includes a pharmaceutical composition which comprises the above antisense oligonucleotide as an active ingredient. The antisense oligonucleotide can also be used to detect such diseases using northern hybridization or PCR.

The present invention also includes a ribozyme which inhibits NF-  $\kappa$  B activation. A ribozyme is an RNA capable of recognizing a nucleotide sequence of a nucleic acid and cleaving the nucleic acid (see e.g., Hiroshi Yanagawa, "Jikken Igaku (Experimental Medicine) Bioscience 12: New Age of RNA). The ribozyme can be produced so that it cleaves the selected target RNA (e.g., mRNA encoding the protein of the present invention). Based on the nucleotide sequence of the DNA encoding the protein of the present invention, the ribozyme specifically cleaving the mRNA of the protein of the present invention can be designed. Such ribozyme has a complementary sequence to the mRNA for the protein of the present invention, complementarily associates with the mRNA and then cleaves the mRNA, which results in reduction or entire loss of the expression of the protein of the present invention. The level of the reduction of the expression is dependent on the level of the ribozyme expression in the target cells.

There are two types of ribozyme commonly used: a hammerhead ribozyme and a hairpin ribozyme. In particular, hammerhead ribozymes have been well studied regarding their primary and secondary structure necessary for their cleavage activity, and those skilled in the art can easily design the ribozymes nucleotided solely on the nucleotide sequence information for the DNA encoding the protein of the present invention [see e.g., Iida et al.,

Saibou Kougaku Vol.16, No.3, p.438-445 (1997); Ohkawa & Taira, Jikken Igaku (Experimental Medicine) Vol.12, No.12, p.83-88 (1994)]. It is known that the hammerhead ribozymes have a structure consisting of two recognition sites (recognition site I and recognition site II forming a chain complementary to target RNA) and an active site, and cleave the target RNA at the 3'end of its sequence NUX (wherein N is A or G or C or U, and X is A or C or U)after the formation of a complementary pair with the target RNA in the recognition sites. In particular, the sequence GUC (or GUA) has been found to have the highest activity [see e.g., Koizumi, M. et al., Nucl. Acids Res. 17:7059-7071 (1989); Iida et al., Saibou Kougaku Vol.16, No.3, p.438-445 (1997); Ohkawa & Taira, Jikken Igaku (Experimental Medicine) Vol.12, No.12, p.83-88 (1994); Kawasaki & Taira, Jikken Igaku (Experimental Medicine) Vol.18, No.3, p.381-386 (2000)].

Therefore the sequence GTC (or GTA) is searched out, and a ribozyme is designed to form several, up to 10 to 20 complementary base pairs around that sequence. The suitability of the designed ribozyme can be evaluated by checking whether the prepared ribozyme can cleave the target mRNA in vitro according to the method described for example in Ohkawa & Taira, Jikken Igaku (Experimental Medicine) Vol.12, No.12, p.83-88 (1994). The ribozyme can be prepared by methods known in the art to synthesize RNA molecules.

Alternatively, the sequence of the ribozyme can be synthesized on a DNA synthesizer and inserted into various vectors containing a suitable RNA polymerase promoter (e.g., T7 or SP6) to enzymatically synthesize an RNA molecule in vitro. Such ribozymes can be introduced into cells by gene transfer methods such as microinjection. Another method involves inserting a ribozyme DNA into a suitable expression vector and introducing the vector into cell strains, cells or tissues. Suitable vectors can be used to introduce the ribozyme into a selected cell. Examples of vectors commonly used for such purpose include plasmid vectors and animal virus vectors (e.g., retrovirus, adenovirus, herpes or vaccinia virus vectors). Such ribozymes are capable of inhibiting the NF- $\kappa$  B activation mediated by the protein of the present invention.

The present invention, moreover, relates to a process for obtaining a new gene

having a function, which comprises using the oligo-capping method to construct a full-length cDNA library, and using a signal factor indicative of the presence of a protein having the function. An example of such signal factor is a reporter gene.

Methods using a cDNA library containing a lot of non-full-length cDNAs are inefficient in obtaining many genes (cDNAs) having functions. Therefore libraries with a high ratio of the number of the full-length cDNA clones to the total number of the clones are necessary. "Full-length cDNA" refers to a complete DNA copy of mRNA from a gene. The cDNA libraries produced using the oligo-capping method contain full-length cDNA clones in a ratio of 50 to 80%, namely, a 5 to 10-fold increase in full-length cDNA clones compared to the cDNA libraries produced by prior art methods (Sumio Sugano, the monthly Full-length cDNA clones are magazine BIO INDUSTRY Vol.16, No.11, p.19-26). essential for protein expression in functional analyses of genes, and full-length cDNA clones themselves are very important materials for activity measurement. Thus, cloning of full-length cDNA is necessary for functional analyses of genes. Sequencing of the cDNA not only provides important information for establishing the primary sequence of the protein encoded by the cDNA, but also reveals the entire exon sequence. Thus, the full-length cDNA provides valuable information for identifying a gene, such as information for determining the primary sequence of a protein, exon-intron structure, the transcription initiation site of mRNA, the location of a promoter, etc.

The construction of full-length cDNA libraries by the oligo-capping method can be carried out, for example, according to the method described in "Shin Idenshi Kougaku Handbook (New Genetic Engineering Handbook)", the third edition (1999), an extra issue of "Jikken Igaku (Experimental Medicine)", YODOSHA CO., LTD. The reporter gene indicative of the presence of a protein having a function contains one or more suitable expression regulation sequence portion to which a protein factor such as a transcriptional factor can bind, and a structural gene portion which allows the measurement of the activation of the proteins factor. The structural gene portion may encode any peptide or protein so long as those skilled in the art can measure the activity or amount of its expression product (including the amount of the mRNA produced). For example,

chloramphenicol acetyltransferase,  $\beta$ -galactosidase, luciferase, etc., can be used and their enzymatic activity measured.

The oligo-capping method used herein involves substituting a cap structure with a synthetic oligo sequence by using BAP, TAP and an RNA ligase, as described in Suzuki & Sugano, "Shin Idenshi Kougaku Handbook (New Genetic Engineering Handbook)", the third edition (1999), an extra issue of "Jikken Igaku (Experimental Medicine)", YODOSHA CO., LTD.

The process of the present invention uses an in vitro system or a cell-based system, preferably a cell-based system. Examples of such cells include cells of prokaryotes such as E. coli, microorganisms such as yeast and fungi, as well as insects and animals. Preferred examples include animal cells, in particular, 293-EBNA cells and NIH3T3 cells.

Examples of reporter genes indicative of the presence of a protein having a function include reporter genes containing a CREB (cAMP responsive element binding protein) binding sequence or AP-1 (activator protein-1) binding sequence at the expression regulation sequence region of the reporter genes, in addition to the NF-  $\kappa$  B reporter genes described herein. For example, if a gene capable of activating CREB is to be obtained, a CREB-dependent reporter plasmid and a full-length cDNA clone produced by the oligo-capping method can be cotransfected into cells, and a plasmid having increased reporter activity can be selected from the cells to attain the purpose. If a gene capable of inhibiting CREB is to be obtained, a CREB-dependent reporter plasmid and a full-length cDNA clone produced by the oligo-capping method can be cotransfected into cells, and a plasmid having decreased reporter activity can be selected from the cells to attain the purpose. These procedures may be carried out in the presence of a certain stimulus to the cells. The cDNA to be transfected into the cells may be a single clone or multiple clones which may be transfected simultaneously. One embodiment of the process of the present invention is detailed in Examples herein. Alternatively, a screening system for obtaining a gene capable of inhibiting NF-  $\kappa$  B activation can also be constructed by cotransfecting a full-length cDNA and a reporter gene into cells and selecting a clone having subnormally increased reporter activity.

However, the process of the present invention is not limited to these embodiments.

Because the cDNA of the present invention is full-length, its 5' end sequence is the transcription initiation site of the corresponding mRNA. Therefore the cDNA sequence can be used to identify the promoter region of the gene by comparing the cDNA with the genomic nucleotide sequence. Genomic nucleotide sequences are available from various databases when the sequences have been deposited in the databases. Alternatively, the cDNA can also be used to clone the desired sequence from a genomic library, for example, Thus, by comparing the by hybridization, and determine its nucleotide sequence. nucleotide sequence of the cDNA of the present invention with a genomic sequence, the promoter fragment thus identified can be used to construct a reporter plasmid for evaluating the expression of the gene. In general, the DNA fragment spanning 2kb (preferably 1kb) upstream from the transcription initiation site can be inserted upstream of the reporter gene to produce the reporter plasmid. The reporter plasmid can be used to screen for a compound which enhances or reduces the expression of the gene. For example, such screening can be carried out by transforming a suitable cell with the reporter plasmid, culturing the transformed cell for a certain period of time, adding a certain amount of a test compound, measuring the reporter activity expressed by the cell after a certain period of time, and comparing the activity with that of a cell to which the test compound has not been These methods are also included in the scope of the present invention. added.

The present invention also relates to a computer-readable medium on which a sequence data set has been stored, said sequence data set comprising at least one nucleotide sequence selected from the group consisting of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175 and 177, and/or at least one amino acid sequence selected from the group consisting of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59,

61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 and 178.

In another aspect, the present invention relates to a method for calculating a homology, which comprises comparing data on the above medium with data of other nucleotide sequences. Thus, the gene and amino acid sequence of the present invention provide valuable information for determining their secondary and tertiary structure, e.g., information for identifying other sequence having a similar function and high homology. These sequences are stored on the computer-readable medium, then a database is searched using data stored in a known macromolecule structure program and a known search tool such as GCG. In this manner, a sequence in a database having a certain homology can be easily found.

The computer-readable medium may be any composition of materials used to store information or data. Examples of such media include commercially available floppy disks, tapes, chips, hard drives, compact disks and video disks. The data on the medium allows a method for calculating a homology by comparing the data with other nucleotide sequence data. This method comprises the steps of providing a first polynucleotide sequence containing the polynucleotide sequence of the present invention for the computer-readable medium, and then comparing the first polynucleotide sequence with at least one-second polynucleotide or polypeptide sequence to identify the homology.

The present invention also relates to an insoluble substrate to which polynucleotide comprising all or part of the nucleotide sequences selected from the group consisting of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175 and 177 are fixed. A plurality of the various polynucleotides which are DNA probes are fixed on a specifically processed solid substrate such as slide glass to form

a DNA microarray and then a labeled target polynucleotide is hybridized with the fixed polynucleotides to detect a signal from each of the probes. The data obtained is analyzed and the gene expression is determined.

The present invention further relates to an insoluble substrate to which polypeptides comprising all or part of the amino acid sequences selected from the group consisting of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 and 178, are fixed. By mixing organism-derived cell extract with the insoluble substrate on which these proteins are fixed, it is possible to isolate or identify cell-derived components such as proteins captured on the insoluble substrate that can be expected to be useful in diagnosis or drug development.

#### Examples:

The following examples further illustrate, but do not limit the present invention.

Example 1: Construction of a full-length cDNA library using the oligo-capping method

(1) Preparation of RNA from human lung fibroblasts (Cryo NHLF)

Human lung fibroblasts (Cryo NHLF: purchased from Sanko Junyaku Co., Ltd.) were cultured according to the attached protocol. After repeating subculturing the cells to obtain fifty 10cm dishes containing the resulting culture, the cells were recovered with a cell scraper. Then, total RNA was obtained from the recovered cells by using the RNA extraction reagent ISOGEN (purchased from NIPPON GENE) according to the manufacturer's protocol. Then, poly A<sup>+</sup> RNA was obtained from the total RNA by using an oligo-dT cellulose column according to Maniatis et al., supra.

(2) Preparation of RNA from mouse ATDC5 cells

ATDC5, a cell strain cloned from mouse EC (embryonal carcinoma) (Atsumi, T. et al.: Cell Diff. Dev., 30: p109-116)(1990) was repeatedly subcultured to obtain fifty 10cm dishes containing the resultant culture. Thereafter, poly A<sup>+</sup> RNA was obtained by a method

similar to that of (1) above.

# (3) Construction of a full-length cDNA library by the oligo-capping method

A full-length cDNA library was constructed from poly A<sup>+</sup> RNA of the above human lung fibroblasts and ATDC5 cells by the oligo-capping method according to the method of Sugano S. et al. [e.g., Maruyama, K. & Sugano, S., Gene, 138:171-174 (1994); Suzuki, Y. et al., Gene, 200:149-156 (1997); Suzuki, Y. & Sugano, S. "Shin Idenshi Kougaku Handbook (New Genetic Engineering Handbook)", the third edition (1999), an extra issue of "Jikken Igaku (Experimental Medicine)", YODOSHA CO., LTD.].

### (4) Preparation of plasmid DNA

The full-length cDNA library constructed as above was transfected into E. coli strain TOP 10 by electroporation, then spread on LB agar medium, and incubated overnight at 37°C. Then, using QIAwell 96 Ultra Plasmid Kit (QIAGEN) according to the manufacturer's protocol, the plasmids were recovered from the colonies grown on ampicillin-containing LB agar medium.

## Example 2: Cloning of DNA capable of activating NF- $\kappa$ B

(1) Screening of the cDNA encoding the protein capable of activating NF-  $\kappa$  B

293-EBNA cells (purchased from Invitrogen) were grown to 1 x  $10^4$  cells/well in a 96 well plate for cell culture for 24 hours at  $37^{\circ}$ C (in the presence of 5% CO<sub>2</sub>) using 5% FBS containing DMEM medium. Then, 50ng of pNF  $\kappa$  B-Luc (purchased from STRATAGENE) and 2  $\mu$  1 of the full-length cDNA prepared in above Example 1.(4) were cotransfected into the cells in a well using FuGENE 6 (purchased from Roche) according to the manufacturer's protocol. After 24 hours of culture at 37°C, the reporter activity of NF- $\kappa$  B (luciferase activity) was measured using long-term luciferase assay system,PIKKA GENE LT2.0 (TOYO INK) according to the attached manufacturer's instructions. The luciferase activity was measured using Wallac ARVO<sup>TM</sup>ST 1420 MULTILABEL COUNTER (Perkin Elmer).

#### (2) DNA sequencing

The above screening was carried out for 155,000 clones, and plasmids showing a 5-fold or more increase in luciferase activity compared to that of the control experiment

(luciferase activity of the cell into which vacant vector pME18S-FL3 is introduced instead of full-length cDNA) were selected. One pass sequencing was carried out from the 5' end of the cloned cDNA (sequencing primer: 5'-CTTCTGCTCTAAAAGCTGCG-3' (SEQ ID NO: 179)) and from the 3' end (sequencing primer: 5'-CGACCTGCAGCTCGAGCACA-3' (SEQ ID NO: 180)) so that as long sequence as possible is determined. The sequencing was carried out using the reagent Thermo Sequenase II Dye Terminator Cycle Sequencing Kit (Amersham Pharmacia Biotech) or BigDye Terminator Cycle Sequencing FS Ready Reaction Kit (Applied Biosystems) and the device ABI PRISM 377 sequencer or ABI PRISM 3100 sequencer according to the manufacturer's instructions.

#### (3) Database analysis of the obtained clones

BLAST (Basic local alignment search tool) searching [S. F. Altschul et al., J. Mol. Biol., 215:403-410 (1990)] was carried out in GenBank for the obtained nucleotide sequence. The results showed that 147 clones represented 89 genes encoding new proteins capable of activating NF-  $\kappa$  B.

#### (4) Full-length sequencing

The full-length DNA sequences for the 89 new clones were determined (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175 and 177). The amino acid sequences of the protein coding regions (open reading frames) were deduced (SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176 and 178).

## Example 3: Screening compounds inhibiting NF- $\kappa$ B activation

293-EBNA cells were seeded on 5% FBS containing DMEM medium in a 96-well cell culture plate to a final cell density of 1 x  $10^4$  cells/ $100\,\mu$  l/well, and cultured for 24

hours at 37°C in the presence of 5% CO<sub>2</sub>. Then, 10ng of the plasmid containing the gene encoding NF-  $\kappa$  B activating protein of SEQ ID NO: 41 and 50ng of the reporter plasmid pNF  $\kappa$  B-Luc were cotransfected into the cells in a well using FuGENE 6. After 1 hour, the proteasome inhibitor MG132 (purchased form CALBIOCHEM) (Uehara T. et al., J. Biol. Chem. 274, p.15875-15882 (1999); Wang X. C. et al., Invest. Ophathalmol. Vis. Sci. 40, p.477-486) was added to the culture to a final concentration of 10  $\mu$  M. After 24 hours of culture at 37°C, the reporter activity was measured using PIKKA GENE LT2.0. The results showed that MG132 inhibited the expression of the reporter gene (Fig. 1).

## **EFFECTS OF THE INVENTION**

As described above, the present invention provides industrially highly useful proteins capable of activating NF-  $\kappa$  B and genes encoding the proteins. The proteins of the present invention and the genes encoding the proteins allow not only screening for compounds useful for treating and preventing diseases associated with the excessive activation or inhibition of NF-  $\kappa$  B, but also production of diagnostics for such diseases. The genes of the present invention are also useful as a gene source used for gene therapy.

#### SEQUENCE LISTING

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<120> Novel Gene

<130> X13-994

<160> 180

<170> Patentin Ver. 2.0

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<211> 167

<212> PRT

<213> Homo sapiens

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Ser Glu Tyr Pro Pro Phe Ser His Arg Tyr Gln Arg Phe Thr Asn Ser 35 40 45

Ala Gly Pro Pro Pro Gly Phe Lys Ser Glu Phe Thr Gly Pro Gln
50 55 60

Asn Thr Gly His Gly Ala Thr Ser Gly Phe Gly Ser Ala Phe Thr Gly 65 70 75 80

Gln Gln Gly Tyr Glu Asn Ser Gly Pro Gly Phe Trp Thr Gly Leu Gly 85 90 95

Thr Gly Gly Ile Leu Gly Tyr Leu Phe Gly Ser Asn Arg Ala Ala Thr 100 105 110

Pro Phe Ser Asp Ser Trp Tyr Tyr Pro Ser Tyr Pro Pro Ser Tyr Pro 115 120 125

Gly Thr Trp Asn Arg Ala Tyr Ser Pro Leu His Gly Gly Ser Gly Ser 130 135 140

Tyr Ser Val Cys Ser Asn Ser Asp Thr Lys Thr Arg Thr Ala Ser Gly
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Tyr Gly Gly Thr Arg Arg Arg 165

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<212> DNA

<213> Homo sapiens

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Tyr Asp Arg Tyr Thr Thr Ser Arg Arg Leu Asp Pro Ile Pro Gln Leu 50 60

Lys Cys Val Gly Gly Thr Ala Gly Cys Asp Ser Tyr Thr Pro Lys Val 65 70 75 80

lle Gln Cys Gln Asn Lys Gly Trp Asp Gly Tyr Asp Val Gln Trp Glu 85 90 95

Cys Lys Thr Asp Leu Asp IIe Ala Tyr Lys Phe Gly Lys Thr Val Val 100 105 110

Ser Cys Glu Gly Tyr Glu Ser Ser Glu Asp Gln Tyr Val Leu Arg Gly 115 120 125

Ser Cys Gly Leu Glu Tyr Asn Leu Asp Tyr Thr Glu Leu Gly Leu Gln 130 135 140

y Lys Gln His Gly Phe Ala Ser Lys Leu Lys Glu Sel 160 Tyr Tyr Tyr Lys Trp Ser Ser Ala Asp Ser Cys Asn Met Ser Gly Leu 170 165 lle Thr lle Val Val Leu Leu Gly lle Ala Phe Val Val Tyr Lys Leu Phe Leu Ser Asp Gly Gln Tyr Ser Pro Pro Pro Tyr Ser Glu Tyr Pro Pro Phe Ser His Arg Tyr Gln Arg Phe Thr Asn Ser Ala Gly Pro Pro Pro Pro Gly Phe Lys Ser Glu Phe Thr Gly Pro Gln Asn Thr Gly His Gly Ala Thr Ser Gly Phe Gly Ser Ala Phe Thr Gly Gln Gln Gly Tyr Glu Asn Ser Gly Pro Gly Phe Trp Thr Gly Leu Gly Thr Gly Gly Ile Leu Gly Tyr Leu Phe Gly Ser Asn Arg Ala Ala Thr Pro Phe Ser Asp Ser Trp Tyr Tyr Pro Ser Tyr Pro Pro Ser Tyr Pro Gly Thr Trp Asn 295 Arg Ala Tyr Ser Pro Leu His Gly Gly Ser Gly Ser Tyr Ser Val Cys 310 Ser Asn Ser Asp Thr Lys Thr Arg Thr Ala Ser Gly Tyr Gly Gly Thr 330 Arg Arg Arg <210> 4 <211> 1924 <212> DNA <213> Homo sapiens <220> <221> CDS <222> (115).. (1131) <400> 4 gttccttcgc cgccgccagg ggtagcggtg tagctgcgca gcgtcgcgcg cgctaccgca 60 117 cccaggttcg gcccgtaggc gtctggcagc ccggcgccat cttcatcgag cgcc atg Met 1 gcc gca gcc tgc ggg ccg gga gcg gcc ggg tac tgc ttg ctc ctc ggc 165

Ala Ala Cys Gly Pro Gly Ala Ala Gly Tyr Cys Leu Leu Leu Gly

| ttg<br>Lei        | g cat<br>u His    | t ttg<br>s Lei<br>20 | ı Phe             | t ctg<br>e Leu    | g ctg<br>ı Leu    | g acc             | gcg<br>Ala<br>25  | Gly               | cct<br>Pro        | gco<br>Ala        | ctg<br>Leu        | g ggo<br>u Gly<br>30 | Trp               | g aad<br>o Asi    | c gac<br>n Asp     | 213 |
|-------------------|-------------------|----------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|----------------------|-------------------|-------------------|--------------------|-----|
| cct<br>Pro        | gac<br>Asp<br>35  | ) Arg                | a atg<br>g Met    | g ttg<br>: Leu    | ctg<br>Leu        | cgg<br>Arg<br>40  | ; Asp             | gta<br>Val        | aaa<br>Lys        | a gct<br>s Ala    | ctt<br>Leu<br>45  | ı Thr                | cto<br>Lei        | cac<br>His        | c tat<br>s Tyr     | 261 |
| gac<br>Asp<br>50  | Arg               | tat<br>Tyr           | acc<br>Thr        | acc<br>Thr        | tcc<br>Ser<br>55  | Arg               | agg<br>Arg        | ctg<br>Leu        | gat<br>Asp        | ccc<br>Pro<br>60  | ) lle             | cca<br>Pro           | cag<br>Glr        | ttg<br>Lei        | g aaa<br>Lys<br>65 | 309 |
| tgt<br>Cys        | gtt<br>Val        | gg <i>a</i><br>Gly   | ggc<br>Gly        | aca<br>Thr<br>70  | Ala               | ggt<br>Gly        | tgt<br>Cys        | gat<br>Asp        | tct<br>Ser<br>75  | Tyr               | acc<br>Thr        | cca<br>Pro           | aaa<br>Lys        | gto<br>Val        |                    | 357 |
| cag<br>G n        | tgt<br>Cys        | cag<br>Gln           | aac<br>Asn<br>85  | Lys               | ggc<br>Gly        | tgg<br>Trp        | gat<br>Asp        | ggg<br>Gly<br>90  | tat<br>Tyr        | gat<br>Asp        | gta<br>Val        | cag<br>G n           | tgg<br>Trp<br>95  | Glu               | tgt<br>Cys         | 405 |
| aag<br>Lys        | acg<br>Thr        | gac<br>Asp<br>100    | Leu               | gat<br>Asp        | att<br>Ile        | gca<br>Ala        | tac<br>Tyr<br>105 | aaa<br>Lys        | ttt<br>Phe        | gga<br>Gly        | aaa<br>Lys        | act<br>Thr<br>110    | gtg<br>Val        | gtg<br>Val        | agc<br>Ser         | 453 |
| tgt<br>Cys        | gaa<br>Glu<br>115 | ggc<br>Gly           | tat<br>Tyr        | gag<br>G u        | tcc<br>Ser        | tct<br>Ser<br>120 | gaa<br>Glu        | gac<br>Asp        | cag<br>Gln        | tat<br>Tyr        | gta<br>Val<br>125 | cta<br>Leu           | aga<br>Arg        | ggt<br>Gly        | tct<br>Ser         | 501 |
| tgt<br>Cys<br>130 | ggc<br>Gly        | ttg<br>Leu           | gag<br>Glu        | tat<br>Tyr        | aat<br>Asn<br>135 | tta<br>Leu        | gat<br>Asp        | tat<br>Tyr        | aca<br>Thr        | gaa<br>Glu<br>140 | ctt<br>Leu        | ggc<br>Gly           | ctg<br>Leu        | cag<br>Gln        | aaa<br>Lys<br>145  | 549 |
| ctg<br>Leu        | aag<br>Lys        | gag<br>Glu           | tct<br>Ser        | gga<br>Gly<br>150 | aag<br>Lys        | cag<br>Gln        | cac<br>His        | ggc<br>Gly        | ttt<br>Phe<br>155 | gcc<br>Ala        | tct<br>Ser        | ttc<br>Phe           | tct<br>Ser        | gat<br>Asp<br>160 | tat<br>Tyr         | 597 |
| tat<br>Tyr        | tat<br>Tyr        | aag<br>Lys           | tgg<br>Trp<br>165 | tcc<br>Ser        | tcg<br>Ser        | gcg<br>Ala        | Asp               | tcc<br>Ser<br>170 | tgt<br>Cys        | aac<br>Asn        | atg<br>Met        | agt<br>Ser           | gga<br>Gly<br>175 | Leu               | att<br>Ile         | 645 |
| acc<br>Thr        | atc<br>lle        | gtg<br>Val<br>180    | gta<br>Val        | ctc<br>Leu        | ctt<br>Leu        | ggg<br>Gly        | atc<br>lle<br>185 | gcc<br>Ala        | ttt<br>Phe        | gta<br>Val        | gtc<br>Val        | tat<br>Tyr<br>190    | aag<br>Lys        | ctg<br>Leu        | ttc<br>Phe         | 693 |
| ctg<br>Leu        | agt<br>Ser<br>195 | gac<br>Asp           | ggg<br>Gly        | cag<br>Gin        | Tyr               | tct<br>Ser<br>200 | cct<br>Pro        | cca<br>Pro        | ccg<br>Pro        | tac<br>Tyr        | tct<br>Ser<br>205 | gag<br>Glu           | tat<br>Tyr        | cct<br>Pro        | cca<br>Pro         | 741 |
| ttt<br>Phe<br>210 | tcc<br>Ser        | cac<br>His           | cgt<br>Arg        | tac<br>Tyr        | cag<br>Gln<br>215 | aga<br>Arg        | ttc<br>Phe        | acc<br>Thr        | Asn               | tca<br>Ser<br>220 | gca<br>Ala        | gga<br>Gly           | cct<br>Pro        | cct<br>Pro        | ccc<br>Pro<br>225  | 789 |
| cca<br>Pro        | ggc<br>Gly        | ttt<br>Phe           | Lys               | tct<br>Ser<br>230 | gag<br>Glu 1      | ttc<br>Phe        | aca<br>Thr        | Gly∣              | cca<br>Pro<br>235 | cag<br>GIn        | aat<br>Asn        | act<br>Thr           | ggc<br>Gly        | cat<br>His<br>240 | ggt<br>Gly         | 837 |

| gca act tct ggt ttt c agt gct ttt aca gga caa caa ggt tat gaa 885<br>Ala Thr Ser Gly Phe Gly Ser Ala Phe Thr Gly Gln Gln Gly Tyr Glu<br>245 250 255    |   |
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| gga tat ttg ttt ggc agc aat aga gcg gca aca ccc ttc tca gac tcg Gly Tyr Leu Phe Gly Ser Asn Arg Ala Ala Thr Pro Phe Ser Asp Ser 275 280 285            |   |
| tgg tac tac ccg tcc tat cct ccc tcc tac cct ggc acg tgg aat agg Trp Tyr Tyr Pro Ser Tyr Pro Pro Ser Tyr Pro Gly Thr Trp Asn Arg 290 295 300 305        | J |
| gct tac tca ccc ctt cat gga ggc tcg ggc agc tat tcg gta tgt tca 1077<br>Ala Tyr Ser Pro Leu His Gly Gly Ser Gly Ser Tyr Ser Val Cys Ser<br>310 315 320 |   |
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45

| gcc<br>Ala                                    | cgt<br>Arg                                      | aag<br>Lys<br>55           | Asn  | cat<br>His   | cac<br>His                            | aag<br>Lys                                   | aca<br>Thr<br>60        | Lys   | tgg<br>Trp                | ttc<br>Phe                     | gtg<br>Val                                   | cct<br>Pro<br>65       | tgg<br>Trp  | gga<br>Gly                                   | ccc<br>Pro                            | 428 |
|---|---|----------------------------|--|--|---------------------------------------|--|-------------------------|---|---------------------------|--------------------------------|--|------------------------|---|--|---------------------------------------|-----|
| aat<br>Asn                                    | cat<br>His<br>70                                | Cys                        | gac<br>Asp                                   | aag<br>Lys   | atc<br>  e                            | cga<br>Arg<br>75                             | gac<br>Asp              | att<br>lle  | gaa<br>G u                | gag<br>G u                     | gca<br>Ala<br>80                             | att<br>Ile             | cca<br>Pro  | agg<br>Arg                                   | gaa<br>G u                            | 476 |
| att<br>lle<br>85                              | Glu   | gcc<br>Ala                 | aat<br>Asn                                   | gac<br>Asp   | atc<br>Ile<br>90                      | gtg<br>Val                                   | ttt<br>Phe              | tct<br>Ser  | gtt<br>Val                | cac<br>His<br>95               | att<br>lle                                   | ccc<br>Pro             | ctc<br>Leu  | ccc<br>Pro                                   | cac<br>His<br>100                     | 524 |
| atg<br>Met                                    | gag<br>Glu                                      | atg<br>Met                 | agt<br>Ser                                   | cct<br>Pro<br>105  | Trp                                   | ttc<br>Phe                                   | caa<br>G n              | ttc<br>Phe  | atg<br>Met<br>110         | ctg<br>Leu                     | ttt<br>Phe                                   | atc<br>He              | ctg<br>Leu  | cag<br>Gln<br>115                            | ctg<br>Leu                            | 572 |
| gac<br>Asp                                    | att<br>He                                       | gcc<br>Ala                 | ttc<br>Phe<br>120                            | aag<br>Lys   | cta<br>Leu                            | aac<br>Asn                                   | aac<br>Asn              | caa<br>Gln<br>125                                   | atc<br>Ile                | agt<br>Ser                     | taa  | gtgta                  | act   | ctcc   | tctcat                                | 625 |
| ccc   | tttc  | ttc d                      | cctt   | tgag   | ca t                                  | tgcc   | ctct                    | t tg  | ggtto                     | cttt                           | ttga   | agcca                  | aat   | tcta   | ataaaa                                | 685 |
| gta   | aaaa  | tgg t                      | taata  | agt  |                                       |  |                         |   |                           |                                |  |                        |   |  |                                       | 702 |
| <pre></pre>                                   |   |                            |  |  |                                       |  |                         |   |                           |                                |  |                        |   |  |                                       |     |
|   |   |                            | sapie  | ens  |                                       |  |                         |   |                           |                                |  |                        |   |  |                                       |     |
| <213<br><400                                  | 3> Ho<br>O> 7                                   | omo s                      |  |  | lle                                   | Glu  | Asn                     | Met   | Ser<br>10                 | Thr                            | Lys  | Lys                    | Leu   | Cys<br>15                                    | lle                                   |     |
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| <21;<br><400<br>Met<br>1<br>Val               | 3> Ho<br>0> 7<br>Ala<br>Gly                     | Gly<br>Gly                 | Ala<br>Ile<br>20                             | lle<br>5<br>Leu  |                                       | Val  | Phe                     | G n<br>25   | 10                        | lle                            | Ala  | Phe                    | Leu<br>30   | 15<br>Val                                    | Gly                                   |     |
| <21; <400 Met 1 Val                           | 3> Ho<br>0> 7<br>Ala<br>Gly<br>Leu              | Gly Gly Ile 35             | Ala<br>Ile<br>20<br>Ala                      | lle<br>5<br>Leu<br>Pro                                   | Leu                                   | Val<br>Pro                                   | Phe<br>Thr<br>40        | Gln<br>25<br>Thr                                    | 10<br>He<br>Ala           | lle<br>Val                     | Ala<br>Ser                                   | Phe<br>Tyr<br>45       | Leu<br>30<br>Met                                    | 15<br>Val<br>Ser                             | Gly<br>Val                            |     |
| <21; <400 Met 1 Val Gly Lys                   | 3> Ho<br>0> 7<br>Ala<br>Gly<br>Leu<br>Cys<br>50 | Gly Gly Ile 35             | Ala<br>Ile<br>20<br>Ala<br>Asp               | lle<br>5<br>Leu<br>Pro<br>Ala                            | Leu<br>Gly                            | Val<br>Pro<br>Lys<br>55                      | Phe<br>Thr<br>40<br>Asn | Gln<br>25<br>Thr<br>His                             | 10<br>His                 | lle<br>Val<br>Lys              | Ala<br>Ser<br>Thr<br>60                      | Phe Tyr 45 Lys         | Leu<br>30<br>Met<br>Trp                             | 15<br>Val<br>Ser<br>Phe                      | Gly<br>Val                            |     |
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| <21: <400 Met  1 Val  Gly  Lys  Pro 65 Ile    | 3> Ho 0> 7 Ala Gly Leu Cys 50 Trp Pro           | Gly Gly Ile 35 Val Gly Arg | Ala<br>Ile<br>20<br>Ala<br>Asp<br>Pro<br>Glu | lle<br>5<br>Leu<br>Pro<br>Ala<br>Asn<br>Ile<br>85        | Leu<br>Gly<br>Arg<br>His<br>70        | Val<br>Pro<br>Lys<br>55<br>Cys               | Phe Thr 40 Asn Asp      | Gln<br>25<br>Thr<br>His<br>Lys                      | 10 His His                | Val<br>Lys<br>Arg<br>75<br>Val | Ala<br>Ser<br>Thr<br>60<br>Asp               | Phe Tyr 45 Lys Ile Ser | Leu<br>30<br>Met<br>Trp<br>Glu<br>Val               | Val<br>Ser<br>Phe<br>Glu<br>His<br>95        | Gly<br>Val<br>Val<br>Ala<br>80        |     |
| <21: <400 Met 1 Val Gly Lys Pro 65 Ile Pro    | 3> Ho 0> 7 Ala Gly Leu Cys 50 Trp Pro           | Gly Gly Ile 35 Val Gly Arg | Ala Ile 20 Ala Asp Pro Glu His 100           | lle<br>5<br>Leu<br>Pro<br>Ala<br>Asn<br>Ile<br>85<br>Met | Leu<br>Gly<br>Arg<br>His<br>70<br>Glu | Val<br>Pro<br>Lys<br>55<br>Cys<br>Ala<br>Met | Phe Thr 40 Asn Asp Asn  | Gln<br>25<br>Thr<br>His<br>Lys<br>Asp<br>Pro<br>105 | 10 Ile Ala His Ile 90 Trp | Val<br>Lys<br>Arg<br>75<br>Val | Ala<br>Ser<br>Thr<br>60<br>Asp<br>Phe<br>Gln | Phe Tyr 45 Lys Ile Ser | Leu<br>30<br>Met<br>Trp<br>Glu<br>Val<br>Met<br>110 | Val<br>Ser<br>Phe<br>Glu<br>His<br>95<br>Leu | Gly<br>Val<br>Val<br>Ala<br>80<br>Ile |     |

| Phe Ala Glu Trp Thr Glu Met Ala His Glu Arg Val Pro Arg Lys Leu<br>145 150 150 160   |                   |
|--|-------------------|
| Lys Cys Thr Phe Thr Ser Pro Lys Thr Pro Glu His Glu Gly Arg Tyr<br>165 170 175   |                   |
| Tyr Glu Cys Asp Val Leu Pro Tyr Ala Gln His Leu His His Tyr Gly<br>180 185 190   |                   |
| Val Val Leu Glu Glu Asp His His Asp Val Pro Thr Pro Ser Ala Ser<br>195 200 205   |                   |
| Gly Lys Ser His Leu Cys Pro Trp Asp Phe His Asp Leu Tyr Gln Tyr<br>210 215 220   |                   |
| Pro Ser Gly Met Val Phe His Arg Val<br>225 230   |                   |
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| acaatcacag ctccgggcat tgggggaacc cgagccggct gcgccggggg aatccgtgcggggccttcc gtcccggtcc catcctcgcc gcgctccagc acctctgaag ttttgcagcg  | g 120             |
| acaatcacag ctccgggcat tgggggaacc cgagccggct gcgccggggg aatccgtgcgggggccttcc gtcccggtcc catcctcgcc gcgctccagc acctctgaag ttttgcagcgcccagaaaagg aggcgaggaa ggagggagtg tgtgagagga gggagcaaaa agctcacccaaaaacattta tttcaaggag aaaagaaaaa ggggggggcgc aaaa atg gct ggg gca Met Ala Gly Ala  | 120<br>180        |
| acaatcacag ctccgggcat tgggggaacc cgagccggct gcgccggggg aatccgtgcgggggccttcc gtcccggtcc catcctcgcc gcgctccagc acctctgaag ttttgcagcgcccagaaagg aggcgaggaa ggagggagtg tgtgagagga gggagcaaaa agctcacccaaaaacattta tttcaaggag aaaagaaaaa ggggggggcgc aaaa atg gct ggg gca Met Ala Gly Ala 1  att ata gaa aac atg agc acc aag aag ctg tgc att gtt ggt ggg att le le Glu Asn Met Ser Thr Lys Lys Leu Cys le Val Gly Gly ile   | 120<br>180<br>236 |
| acaatcacag ctccgggcat tgggggaacc cgagccggct gcgccggggg aatccgtgcggggccttcc gtcccggtcc catcctcgcc gcgctccagc acctctgaag ttttgcagcgcccagaaagg aggcgaggaa ggagggagtg tgtgagagga gggagcaaaa agctcacccaaaaacatta ttcaaggag aaaagaaaaa ggggggggcc aaaa atg gct ggg gca Met Ala Gly Ala 1  att ata gaa aac atg agc acc aag aag ctg tgc att gtt ggt ggg att lie lie Glu Asn Met Ser Thr Lys Lys Leu Cys lie Val Gly Gly lie 5 10 15 20  ctg ctc gtg ttc caa atc atc gcc ttt ctg gtg gga ggc ttg att gct Leu Leu Val Phe Gln lie lie Ala Phe Leu Val Gly Gly Leu lie Ala  | 236<br>284        |
| acaatcacag ctccgggcat tgggggaacc cgagccggct gcgccggggg aatccgtgcgggccttcc gtcccggtcc catcctcgcc gcgctccagc acctctgaag ttttgcagcgcccagaaagg aggcgaggaa ggagggagtg tgtgagagga gggagcaaaa agctcacccaaaaacattta tttcaaggag aaaagaaaaa ggggggggcc aaaa atg gct ggg gca Met Ala Gly Ala 1  att ata gaa aac atg agc acc aag aag ctg tgc att gtt ggt ggg att lie lie Glu Asn Met Ser Thr Lys Lys Leu Cys lie Val Gly Gly lie 5 10 15 20  ctg ctc gtg ttc caa atc atc gcc ttt ctg gtg gga ggc ttg att gct Leu Leu Val Phe Gln lie lie Ala Phe Leu Val Gly Gly Leu lie Ala 25 30 35  cca ggg ccc aca acg gca gtg tcc tac atg tcg gtg aaa tgt gtg gat Pro Gly Pro Thr Thr Ala Val Ser Tyr Met Ser Val Lys Cys Val Asp | 236<br>284<br>332 |

|      | gaa<br>Glu        |       |       |       |       |       |       |       |       |       |       |       |       |       |        | 524  |
|------|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|--------|------|
|      | gag<br>Glu        |       |       |       |       |       |       |       |       |       |       |       |       |       |        | 572  |
|      | att<br>  e        |       |       |       |       |       |       |       |       |       |       |       |       |       |        | 620  |
|      | atg<br>Met        |       |       |       |       |       |       |       |       |       |       |       |       |       |        | 668  |
|      | gaa<br>Glu<br>150 |       |       |       |       |       |       |       |       |       |       |       |       |       |        | 716  |
|      | tct<br>Ser        |       |       |       |       |       |       |       |       |       |       |       |       |       |        | 764  |
|      | ctt<br>Leu        |       |       |       |       |       |       |       |       |       |       |       |       |       |        | 812  |
|      | gat<br>Asp        |       |       |       |       |       |       |       |       |       |       |       |       |       |        | 860  |
|      | tgc<br>Cys        |       |       |       |       |       |       |       |       |       |       |       |       |       |        | 908  |
|      | ttc<br>Phe<br>230 |       |       |       | tgad  | tgga  | acc t | ggat  | gctg  | gc tg | gtttg | ggtga | a cat | ccga  | acag   | 963  |
| ggca | atctt             | ct a  | atgcg | gatgo | t to  | etgto | ctto  | tgg   | gatca | atct  | tctg  | gtggo | ga g  | gcaca | atgatg | 1023 |
| gato | cagca             | acg a | agcgg | gaaco | ca ca | atcgo | aggg  | g tat | ttgga | aagc  | aagt  | tcgga | acc ( | catte | gccgtt | 1083 |
| ggc  | tcctt             | ct g  | gccto | ettea | at at | ttga  | acate | g tgt | tgaga | agag  | gggt  | acaa  | act o | cacga | atccc  | 1143 |
| ttct | tacag             | gta t | ctgg  | gacta | ac ag | gacat | tgga  | aca   | agago | tgg   | ccat  | ggco  | ctt o | catca | atcgtg | 1203 |
| gct  | ggaat             | ct g  | gooto | ctgcc | ct ct | actt  | ccte  | g ttt | ctat  | gct   | tcat  | ggta  | att t | cage  | gtgttt | 1263 |
| cgga | aacat             | ca g  | gtggg | gaago | a gt  | ccag  | gcctg | g cca | agcta | atga  | gcaa  | aagto | cg g  | gegge | tacac  | 1323 |
| tat  | gaggg             | ggc t | aatt  | ttta  | ag gt | tcaa  | agtto | cto   | catgo | tta   | tcad  | ctte  | ggc o | etgcg | ctgcc  | 1383 |
| atga | actgt             | ca t  | ctto  | cttca | at cg | gttag | gtcag | g gta | acge  | gaag  | gcca  | attgg | gaa a | atggg | gcggc  | 1443 |

gtcacagtcc aagtgaac tgcctttttc acaggcatct atgggatgt aatctgtat 1503 gtotttgoto tgatgttott gtatgoacca toccataaaa actatggaga agaccagtoo 1563 aatggcgatc tgggtgtcca tagtggggaa gaactccagc tcaccaccac tatcacccat 1623 gtggacggac ccactgagat ctacaagttg acccgcaagg aggcccagga gtaggaggct 1683 gcagcgcccg gctgggacgg tctctccata ccccagcccc tctaactaga gtggggagca 1743 tgccagagag agctcaatgt acaaatgaat gcctcatggc tcttagctgt ggtttcttgg 1803 accagcggca tggacatttg tcagtttgcc ttctgacggt agcttttgga ggaagattcc 1863 tgcagccact aatgcattgt gtatgataac aaaaactctg gtatgacaca ttttctgtga 1923 tcattgttaa ttagtgacat agtaacatct gtagcagctg gttagtaaac ctcatgtggg 1983 ggtggggtgg gggtgtattc cttgggggat ggtttgggcc gaatggggag tggaatattt 2043 gacatttttc ctgttttaaa ttctaggata gattttaaca tcctttgcgg tcccagtcca 2103 aggtaggctg gtgtcatagt cttctcactc ctaatccatg accactgttt ttttcctatt 2163 tatatcacca ggtagcccac tgagttaata tttaagttgt caatagataa gtgtccctgt 2223 tttgtggcat aatataactg aatttcatga gaagatttat tccaccaggg gtatttcagc 2283 tttgaaacca aatctgtgta tctaatacta accaatctgt tggatgtggg ttttaaaaaa 2343 tgtttgctaa actacccaag taagatttac tgtattaaat ggccttcggg tctgaaaagc 2403 ttttt 2409

<sup>&</sup>lt;210> 9

<sup>&</sup>lt;211> 198

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

<sup>&</sup>lt;400> 9

Met Ala Thr Leu Trp Gly Gly Leu Leu Arg Leu Gly Ser Leu Leu Ser 1 5 10 15

Leu Ser Cys Leu Ala Leu Ser Val Leu Leu Leu Ala Gin Leu Ser Asp 20 25 30

Ala Ala Lys Asn Phe Glu Asp Val Arg Cys Lys Cys IIe Cys Pro Pro 35 40 45

Tyr Lys Glu Asn Ser Gly His IIe Tyr Asn Lys Asn IIe Ser Gln Lys 50 55 60

Asp Cys Asp Cys Leu His Val Val Glu Pro Met Pro Val Arg Gly Pro 65 70 75 80

Asp Val Glu Ala Tyr Cys Leu Arg Cys Glu Cys Lys Tyr Glu Glu Arg 85 90 95

| •  | Thr lle<br>100  | Lys Val  | Thr   | lle<br>105   | lle  | lle   | Tyr  | Leu  | Ser<br>110   | lle  | Leu  |   |  |
|--|---|--|---|--|--|---|--|--|--|--|--|---|--|
| Gly Leu Leu l<br>115   | Leu Leu   | Tyr Met  | Val<br>120  | Tyr  | Leu  | Thr   | Leu  | Va l<br>125  | Glu  | Pro  | He   |   |  |
| Leu Lys Arg /<br>130   | Arg Leu   | Phe Gly  |   | Ala  | Gln  | Leu   | lle<br>140   | Gln  | Ser  | Asp  | Asp  |   |  |
| Asp lle Gly /<br>145   | Asp His   | Gln Pro<br>150   | Phe   | Ala  | Asn  | Ala<br>155  | His  | Asp  | Val  | Leu  | Ala<br>160   |   |  |
| Arg Ser Arg S  | Ser Arg<br>165  | Ala Asr  | Val   | Leu  | Asn<br>170   | Lys   | Val  | Glu  | Tyr  | Ala<br>175   | Gln  |   |  |
| Gin Arg Trp I  | Lys Leu<br>180  | Gin Val  | Gln   | Glu<br>185   | Gln  | Arg   | Lys  | Ser  | Val<br>190   | Phe  | Asp  |   |  |
| Arg His Val V<br>195   | Val Leu   | Ser  |   |  |  |   |  |  |  |  |  |   |  |
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| <212> DNA<br><213> Homo sapiens<br><220><br><221> CDS<br><222> (86) (679)  |   |  |   |  |  |   |  |  |  |  |  |   |  |
| <pre>&lt;222&gt; (86) (679)  &lt;400&gt; 10 gtgcctgagc ctgagcctga gcctgagccc gagccgggag ccggtcgcgg gggctccggg 6</pre>          |   |  |   |  |  |   |  |  |  |  |  |   |  |
| <400> 10   | ~   | ga gcctg   | agcc  | c gaş  | gccgg  | ggag  | ccgg   | gtogo  | gg g   | gggct  | ccggg  | 60  |  |
| <400> 10   | tgagcct   |  | atg   | gcg  |  | ctg   | tgg  | gga  | ggc  | ctt  | ctt  | 60<br>112                                     |  |
| <400> 10<br>gtgcctgagc c   | tgagcctgctgctggccc  | ctc agc  | atg<br>Met<br>1   | gcg<br>Ala   | acc<br>Thr   | ctg<br>Leu<br>ctg                                   | tgg<br>Trp<br>5  | gga<br>Gly<br>ctt                                    | ggc<br>Gly<br>tcc  | ctt<br>Leu<br>gtg  | ctt<br>Leu<br>ctg  |   |  |
| <pre>&lt;400&gt; 10 gtgcctgagc c ctgtgggacc gc cgg ctt ggc f Arg Leu Gly S</pre>   | tgagcctgctggcco   | ctc ago<br>Leu Ser<br>15   | atg<br>Met<br>1<br>ctg<br>Leu                             | gcg<br>Ala<br>tcg<br>Ser                                   | acc<br>Thr<br>tgc<br>Cys                                   | ctg<br>Leu<br>ctg<br>Leu<br>20                      | tgg<br>Trp<br>5<br>gcg<br>Ala                          | gga<br>Gly<br>ctt<br>Leu                             | ggc<br>Gly<br>tcc<br>Ser                                   | ctt<br>Leu<br>gtg<br>Val                                   | ctt<br>Leu<br>ctg<br>Leu<br>25                             | 112   |  |
| <pre>&lt;400&gt; 10 gtgcctgagc c ctgtgggacc gc cgg ctt ggc c Arg Leu Gly 3 10 ctg ctg gcg c</pre>                              | tgagcctgctggccctcc ttg<br>Ser Leucag ctg<br>Gin Leu<br>30                                 | ctc ago<br>Leu Ser<br>15<br>tca gao<br>Ser Asp                       | atg<br>Met<br>1<br>ctg<br>Leu<br>gcc                      | gcg<br>Ala<br>tcg<br>Ser<br>gcc<br>Ala                     | acc<br>Thr<br>tgc<br>Cys<br>aag<br>Lys<br>35<br>gaa        | ctg<br>Leu<br>ctg<br>Leu<br>20<br>aat<br>Asn        | tgg<br>Trp<br>5<br>gcg<br>Ala<br>ttc<br>Phe            | gga<br>Gly<br>ctt<br>Leu<br>gag<br>Glu               | ggc<br>Gly<br>tcc<br>Ser<br>gat<br>Asp                     | ctt<br>Leu<br>gtg<br>Val<br>gtc<br>Val<br>40<br>att        | ctt<br>Leu<br>ctg<br>Leu<br>25<br>aga<br>Arg               | 112<br>160                                    |  |
| <pre>&lt;400&gt; 10 gtgcctgagc cf ctgtgggacc gc cgg ctt ggc f Arg Leu Gly 3 10 ctg ctg gcg c Leu Leu Ala c tgt aaa tgt a</pre> | tgagcctgctggccctcc ttg<br>Ser Leu<br>cag ctg<br>GIn Leu<br>30<br>atc tgc<br>IIe Cys<br>45 | ctc ago<br>Leu Ser<br>15<br>tca gao<br>Ser Asp<br>cct ccc<br>Pro Pro | atg<br>Met<br>1<br>ctg<br>Leu<br>gcc<br>Ala<br>tat<br>Tyr | gcg<br>Ala<br>tcg<br>Ser<br>gcc<br>Ala<br>aaa<br>Lys<br>50 | acc<br>Thr<br>tgc<br>Cys<br>aag<br>Lys<br>35<br>gaa<br>Glu | ctg<br>Leu<br>ctg<br>Leu<br>20<br>aat<br>Asn<br>aat | tgg<br>Trp 5<br>gcg<br>Ala<br>ttc<br>Phe<br>tct<br>Ser | gga<br>Gly<br>ctt<br>Leu<br>gag<br>Glu<br>ggg<br>Gly | ggc<br>Gly<br>tcc<br>Ser<br>gat<br>Asp<br>cat<br>His<br>55 | ctt<br>Leu<br>gtg<br>Val<br>gtc<br>Val<br>40<br>att<br>Ile | ctt<br>Leu<br>ctg<br>Leu<br>25<br>aga<br>Arg<br>tat<br>Tyr | <ul><li>112</li><li>160</li><li>208</li></ul> |  |

| gaa tgc aaa tat gaa gaa aga agc tct gtc aca atc aag gtt acc att<br>Glu Cys Lys Tyr Glu Glu Arg Ser Ser Val Thr IIe Lys Val Thr IIe<br>90 95 100 105   | 400  |
|---|--|
| ata att tat ctc tcc att ttg ggc ctt cta ctt ctg tac atg gta tat<br>lle lle Tyr Leu Ser lle Leu Gly Leu Leu Leu Leu Tyr Met Val Tyr<br>110 115 120   | 448  |
| ctt act ctg gtt gag ccc ata ctg aag agg cgc ctc ttt gga cat gca<br>Leu Thr Leu Val Glu Pro lle Leu Lys Arg Arg Leu Phe Gly His Ala<br>125 130 135   | 496  |
| cag ttg ata cag agt gat gat gat att ggg gat cac cag cct ttt gca<br>Gln Leu lle Gln Ser Asp Asp Asp lle Gly Asp His Gln Pro Phe Ala<br>140 145 150   | 544  |
| aat gca cac gat gtg cta gcc cgc tcc cgc agt cga gcc aac gtg ctg<br>Asn Ala His Asp Val Leu Ala Arg Ser Arg Ser Arg Ala Asn Val Leu<br>155 160 165   | 592  |
| aac aag gta gaa tat gca cag cag cgc tgg aag ctt caa gtc caa gag<br>Asn Lys Val Glu Tyr Ala Gln Gln Arg Trp Lys Leu Gln Val Gln Glu<br>170 175 180 185   | 640  |
| cag cga aag tot gto ttt gac cgg cat gtt gto otc ago taattgggaa<br>Gln Arg Lys Ser Val Phe Asp Arg His Val Val Leu Ser<br>190 195  | 689  |
|   |  |
| ttgaattcaa ggtgactaga aagaaacagg cagacaactg gaaagaactg actgggttt  | 749  |
| ttgaattcaa ggtgactaga aagaaacagg cagacaactg gaaagaactg actgggttt gctgggtttc attttaatac cttgttgatt tcaccaactg ttgctggaag attcaaaac   |  |
|   | 809  |
| gctgggtttc attttaatac cttgttgatt tcaccaactg ttgctggaag attcaaaac  | 809  |
| gctgggtttc attttaatac cttgttgatt tcaccaactg ttgctggaag attcaaaac<br>ggaagcaaaa acttgcttga ttttttttc ttgttaacgt aataatagag acatttta  | 809<br>869<br>929  |
| gctgggttc atttaatac cttgttgatt tcaccaactg ttgctggaag attcaaaac<br>ggaagcaaaa acttgcttga tttttttc ttgttaacgt aataatagag acatttta<br>aagcacacag ctcaaagtca gccaataagt ctttcctat ttgtgacttt tactaataa  | 809<br>869<br>929<br>989   |
| gctgggttc atttaatac cttgttgatt tcaccaactg ttgctggaag attcaaaac ggaagcaaaa acttgcttga tttttttc ttgttaacgt aataatagag acatttta aagcacacag ctcaaagtca gccaataagt ctttcctat ttgtgactt tactaataa aataaatctg cctgtaaatt atcttgaagt cctttacctg gaacaagcac tctctttt   | 809<br>869<br>929<br>989<br>1049   |
| gctgggtttc atttaatac cttgttgatt tcaccaactg ttgctggaag attcaaaac ggaagcaaaa acttgcttga tttttttc ttgttaacgt aataatagag acatttta aagcacacag ctcaaagtca gccaataagt ctttcctat ttgtgacttt tactaataa aataaatctg cctgtaaatt atcttgaagt cctttacctg gaacaagcac tctctttt accacatagt tttaacttga ctttcaagat aatttcagg gttttgttg ttgttgtt                         | 809<br>869<br>929<br>989<br>1049<br>1109   |
| gctgggtttc attttaatac cttgttgatt tcaccaactg ttgctggaag attcaaaac ggaagcaaaa acttgcttga ttttttttc ttgttaacgt aataatagag acatttta aagcacacag ctcaaagtca gccaataagt ctttcctat ttgtgacttt tactaataa aataaatctg cctgtaaatt atcttgaagt cctttacctg gaacaagcac tctctttttaaccacatagt tttaacttga ctttcaagat aatttcagg gttttgttg ttgttgttt ttgttgttt gtttgttg  | 809<br>869<br>929<br>989<br>1049<br>1109   |
| gctgggtttc attttaatac cttgttgatt tcaccaactg ttgctggaag attcaaaac ggaagcaaaa acttgcttga ttttttttc ttgttaacgt aataatagag acatttta aagcacacag ctcaaagtca gccaataagt ctttcctat ttgtgacttt tactaataa aataaatctg cctgtaaatt atcttgaagt cctttacctg gaacaagcac tctctttttaccacatagt tttaacttga ctttcaagat aattttcagg gttttgttg ttgttgttt ttgttgttt gtttggtgg | 809<br>869<br>929<br>989<br>1049<br>1109<br>1169                                 |
| gctgggtttc attttaatac cttgttgatt tcaccaactg ttgctggaag attcaaaac ggaagcaaaa acttgcttga tttttttc ttgttaacgt aataatagag acatttta aagcacacag ctcaaagtca gccaataagt ctttcctat ttgtgactt tactaataa aataaatctg cctgtaaatt atcttgaagt cctttacctg gaacaagcac tctctttt accacatagt tttaacttga ctttcaagat aatttcagg gttttgttg ttgttgttt ttgttgttt gttttggtgg   | 809<br>869<br>929<br>989<br>1049<br>1109<br>1169<br>1229<br>1289                 |
| gctgggtttc attttaatac cttgttgatt tcaccaactg ttgctggaag attcaaaac ggaagcaaaa acttgcttga tttttttc ttgttaacgt aataatagag acatttta aagcacacag ctcaaagtca gccaataagt ctttcctat ttgtgacttt tactaataa aataaatctg cctgtaaatt atcttgaagt cctttacctg gaacaagcac tctctttt accacatagt tttaacttga ctttcaagat aatttcagg gttttgttg ttgttgtt ttgttgttt gttttgttg    | 809<br>869<br>929<br>989<br>1049<br>1109<br>1169<br>1229<br>1289<br>1349         |
| gctgggttc atttaatac cttgttgatt tcaccaactg ttgctggaag attcaaaac ggaagcaaaa acttgcttga tttttttc ttgttaacgt aataatagag acatttta aagcacacag ctcaaagtca gccaataagt ctttcctat ttgtgactt tactaataa aataaatctg cctgtaaatt atcttgaagt cctttacctg gaacaagcac tctcttttcaccacatagt tttaacttga ctttcaagat aatttcagg gttttgttg ttgttgttt ttgttgttt gtttggtgg      | 809<br>869<br>929<br>989<br>1049<br>1109<br>1169<br>1229<br>1289<br>1349<br>1409 |

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Gin Ala Ala Gly Asp Ala Pro Pro Pro Tyr Ser Ser Ile Ser Ala Glu 35 40 45

Ser Ala Ala Tyr Phe Asp Tyr Lys Asp Glu Ser Gly Phe Pro Lys Pro 50 55 60

Pro Ser Tyr Asn Val Ala Thr Thr Leu Pro Ser Tyr Asp Glu Ala Glu 65 70 75 80

Arg Thr Lys Ala Glu Ala Thr Ile Pro Leu Val Pro Gly Arg Asp Glu 85 90 95

Asp Phe Val Gly Arg Asp Asp Phe Asp Asp Ala Asp Gln Leu Arg Ile 100 105 110

Gly Asn Asp Gly Ile Phe Met Leu Thr Phe Phe Met Ala Phe Leu Phe 115 120 125

Asn Trp lle Gly Phe Phe Leu Ser Phe Cys Leu Thr Thr Ser Ala Ala 130 135 140

Gly Arg Tyr Gly Ala IIe Ser Gly Phe Gly Leu Ser Leu IIe Lys Trp 145 150 155 160

lle Leu lle Val Arg Phe Ser Thr Tyr Phe Pro Gly Tyr Phe Asp Gly 165 170 175

Gln Tyr Trp Leu Trp Trp Val Phe Leu Val Leu Gly Phe Leu Leu Phe 180 185 190

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Phe Ser Asn Leu Pro Arg Thr Arg Val Leu Phe Ile Tyr 210 215 220

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| ccctcggcc tcc                           | cagogot cocaa                         | gccgc agcg                    | gccgcg ccc                      | ccttcagc tago                        | tcgctc 120     |
| gctcgctctg ctt                          | ccctgct gccgg                         |                               |                                 | g gcg ttg gcg<br>u Ala Leu Ala<br>5  |                |
| ctg gcg gcg gt<br>Leu Ala Ala Va<br>10  |                                       |                               |                                 |                                      |                |
| aat gaa gaa ga<br>Asn Glu Glu Gl<br>25  |                                       | Pro Glu G                     |                                 | a Gly Asp Ala                        |                |
| cca cct tac ag<br>Pro Pro Tyr Se<br>40  |                                       |                               |                                 |                                      |                |
| aag gat gag tc<br>Lys Asp Glu Se        | t ggg ttt cca<br>r Gly Phe Pro<br>60  | Lys Pro P                     | ca tot tad<br>Pro Ser Tyr<br>65 | c aat gta gct<br>r Asn Val Ala<br>70 | 1 Thr          |
| aca ctg ccc ag<br>Thr Leu Pro Se<br>7   | r Tyr Asp Glu                         |                               |                                 |                                      |                |
| atc cct ttg gt<br>lle Pro Leu Va<br>90  |                                       |                               |                                 |                                      |                |
| ttt gat gat gc<br>Phe Asp Asp Al<br>105 | t gac cag ctg<br>a Asp GIn Leo<br>110 | Arg lle G                     | ga aat ga<br>ily Asn Asi<br>11  | p Gly lle Phe                        | atg 509<br>Met |
| tta act ttt tt<br>Leu Thr Phe Ph<br>120 |                                       |                               |                                 |                                      |                |
| tct ttt tgc ct<br>Ser Phe Cys Le        |                                       | - Ala Ala G                   |                                 |                                      | e Ser          |
| gga ttt ggt ct<br>Gly Phe Gly Le<br>15  | u Ser Leu IIe                         | aaa tgg a<br>Lys Trp I<br>160 | itc ctg at<br>le Leu IIo        | t gtc agg tt<br>e Val Arg Pho<br>165 | tcc 653<br>Ser |
| acc tat ttc cc<br>Thr Tyr Phe Pr<br>170 |                                       |                               |                                 |                                      |                |
| ttc ctt gtt tt<br>Phe Leu Val Le<br>185 |                                       | ı Leu Phe L                   |                                 | y Phe IIe Asr                        |                |
| gca aaa gtt cg                          | g aag atg cca                         | a gaa act t                   | tc tca aa                       | t ctc ccc agg                        | g acc 797      |

aga gtt ctc ttt att tat taaagatgtt ttctggcaaa ggccttcctg Arg Val Leu Phe lle Tyr 220 845

catttatgaa ttctctctca agaagcaaga gaacacctgc aggaagtgaa tcaagatgca 905 gaacacagag gaataatcac ctgctttaaa aaaataaagt actgttgaaa agatcatttc 965 tctctatttg ttcctaggtg taaaatttta atagttaatg cagaattctg taatcattga 1025 atcattagtg gttaatgttt gaaaaagctc ttgcaatcaa gtctgtgatg tattaataat 1085 gccttatata ttgtttgtag tcattttaag tagcatgagc catgtccctg tagtcggtag 1145 ggggcagtct tgctttattc atcctccatc tcaaaatgaa cttggaatta aatattgtaa 1205 gatatgtata atgctggcca ttttaaaggg gttttctcaa aagttaaact tttgctatga 1265 ctgtgttttt gcacataatc catatttgct gttcaagtta atctagaaat ttattcaatt 1325 ctgtatgaac acctggaagc aaaatcatag tgcaaaaata catttaaggt gtggtcaaaa 1385 ataagtottt aattggtaaa taataagoat taatttttta tagootgtat toacaattot 1445 gcggtacctt attgtaccta agggattcta aaggtgttgt cactgtataa aacagaaagc 1505 actaggatac aaatgaagct taattactaa aatgtaattc ttgacactct ttctataatt 1565 . agogttotto accoccacco coaccoccac coccettatt ttoottttgt ctcctggtga 1625 ttaggccaaa gtctgggagt aaggaggagta ttaggtactt aggagcaaag aaagaagtag 1685 cttggaactt ttgagatgat ccctaacata ctgtactact tgcttttaca atgtgttagc 1745 agaaaccagt gggttataat gtagaatgat gtgctttctg cccaagtggt aattcatctt 1805 ggtttgctat gttaaaactg taaatacaac agaacattaa taaatatctc ttgtgtagc 1864

<sup>&</sup>lt;210> 13

<sup>&</sup>lt;211> 242

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

<sup>&</sup>lt;400> 13

Met Asp His His Gln Pro Gly Thr Gly Arg Tyr Gln Val Leu Leu Asn 1 5 10 15

Glu Glu Asp Asn Ser Glu Ser Ser Ala IIe Glu Gln Pro Pro Thr Ser 20 25 30

Asn Pro Ala Pro Gln Ile Val Gln Ala Ala Ser Ser Ala Pro Ala Leu 35 40 45

Glu Thr Asp Ser Ser Pro Pro Pro Tyr Ser Ser Ile Thr Val Glu Val

55

Pro Thr Thr Ser Asp Thr Glu Val Tyr Gly Glu Phe Tyr Pro Val Pro 65 70 75 80

Pro Pro Tyr Ser Val Ala Thr Ser Leu Pro Thr Tyr Asp Glu Ala Glu 85 90 95

Lys Ala Lys Ala Ala Ala Met Ala Ala Ala Ala Ala Glu Thr Ser Gln 100 105 110

Arg Ile Gln Glu Glu Glu Cys Pro Pro Arg Asp Asp Phe Ser Asp Ala 115 120 125

Asp Gln Leu Arg Val Gly Asn Asp Gly lie Phe Met Leu Ala Phe Phe 130 135 140

Met Ala Phe lle Phe Asn Trp Leu Gly Phe Cys Leu Ser Phe Cys lle 145 150 155 160

Thr Asn Thr lie Ala Gly Arg Tyr Gly Ala lie Cys Gly Phe Gly Leu 165 170 175

Ser Leu lle Lys Trp lle Leu lle Val Arg Phe Ser Asp Tyr Phe Thr 180 185 190

Gly Tyr Phe Asn Gly Gln Tyr Trp Leu Trp Trp Ile Phe Leu Val Leu 195 200 205

Gly Leu Leu Phe Phe Arg Gly Phe Val Asn Tyr Leu Lys Val Arg 210 215 220

Asn Met Ser Glu Ser Met Ala Ala Ala His Arg Thr Arg Tyr Phe Phe 225 230 235 240

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<211> 2324

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<400> 14

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ctt ctt aat gaa gag gat aac tca gaa tca tcg gct ata gag cag cca 99 Leu Leu Asn Glu Glu Asp Asn Ser Glu Ser Ser Ala Ile Glu Gln Pro 15 20 25

cct act tca aac cca gca ccg cag att gtg cag gct gcg tct tca gca 147

| Pro<br>30  | Thr               | Ser        | Asn        | Prd               | 35         | Pro        | Gln        | lle        | Val               | Gln<br>40  | Ala        | Ala        |            | Ser               | Ala<br>45  |     |
|------------|-------------------|------------|------------|-------------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|-------------------|------------|-----|
|            | gca<br>Ala        |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |            | 195 |
|            | gaa<br>Glu        |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |            | 243 |
|            | gtg<br>Val        |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |            | 291 |
|            | gct<br>Ala<br>95  |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |            | 339 |
|            | tct<br>Ser        |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |            | 387 |
| agt<br>Ser | gat<br>Asp        | gca<br>Ala | gac<br>Asp | cag<br>Gln<br>130 | ctc<br>Leu | aga<br>Arg | gtg<br>Val | ggg<br>Gly | aat<br>Asn<br>135 | gat<br>Asp | ggc<br>Gly | att<br>lle | ttc<br>Phe | atg<br>Met<br>140 | ctg<br>Leu | 435 |
|            | ttt<br>Phe        |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |            | 483 |
|            | tgt<br>Cys        |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |            | 531 |
|            | ggc<br>Gly<br>175 |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |            | 579 |
|            | ttt<br>Phe        |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |            | 627 |
|            | gta<br>Val        |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |            | 675 |
|            | gtc<br>Val        |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |            | 723 |
|            | ttc<br>Phe        |            |            |                   | taga       | agact      | tgc a      | atcaa      | accc              | ga ca      | attco      | ettte      | tta        | ataco             | caat       | 778 |
| gte        | aaat              | ttc (      | cagat      | tcato             | ct gt      | taaad      | cctad      | c aac      | ottta             | aata       | gaag       | gacta      | act a      | aataa             | acagaa     | 838 |
| gac        | aaat              | tag †      | tgaag      | gaaaa             | ag ac      | cggag      | gttt       | c gaa      | atte              | gaat       | ggca       | agggt      | tgg 1      | tttt              | tgctta     | 898 |

caagccattt ctgttcattc tttaagtatc tatatttcat ttgttttgca catatgcata 958 tgtgcccatt taagatattt gcatatactt gatagaaacc ataaagttgt agcagttaag 1018 tccagtcaca tttggttaat cagtgtttga tataattgaa agagttgagt ggataaacag 1078 tcttccagct tgtaaatgcc attgacttct gacctgacat ttagtataat aaaaatgaaa 1138 ttcttaacca tgtcaaatga tttagtttct ggctcttaga ctcatctggc agttctacac 1198 atgaaacatc ttttgttata tagggtgtat tgaaacctgc agtgctgatt attagaaagg 1258 atttgtcaga tttttgaaca tgatatttac attattattt aggaaaactc ttcctgtaaa 1318 taaccatgca taacttactt tctgcaatgt tttcttagaa attgtgtcca gatagctttc 1378 actaatttta aattaagtga actaaatata tatgtgtata tgtatacaca tatataca 1438 cacacacata tatatatta gaaacgtgag tgttaaagat agaatttgtt ttaggacaaa 1498 ttttaagaaa atgtgggaat accaaatgtc ctttataaga aaaataaatt ttatttaag 1558 ggacatacta gttttaggga ttttcagatg ggaagctgca tttttaggat tgcccatctt 1618 tcaaagttaa ttttctaaat aagataattc tcatttgtgt ttgtctttta aaaggccaat 1738 aaaatatott toagtatoat tgtaataatt ttttagagtt taatttgtaa agottagoaa 1798 ataaaatott gtactatgaa tagottottg otttatgact ttaggattaa ottgtaaaaa 1858 acatatcctg aactgagata tgcaaaatac tcattttcaa gttatggaaa tgtgtttgtg 1918 gcatatagga ctgtggggtc tgtgtgtgta gtgagagtgt gtagccacta ttataactgg 1978 aatttaattt acattcataa actactatat ttcccatctt gcaaatcatt ttatgtctca 2038 tctgtttttc ctttcggtta tatctttggt tttgaatacc aacatttaaa atgatggtat 2098 tttatctttt aaacttaaaa attatttaat acagctatat ggaccttata aaattgattt 2158 cttatttatt attagacatt actactaaaa ggtacatcta actattcagg gacattttc 2218 catttccaaa aaataaaatt tattatgctt tataacctct tctgtatttt ctaattttt 2278 2324 cattgtcttt gataaataaa acagttttgt tttgctaata tagcct

<sup>&</sup>lt;210> 15

<sup>&</sup>lt;211> 242

<sup>212&</sup>gt; PRT

<sup>&</sup>lt;213> Homo sapiens

<sup>&</sup>lt;400> 15

Met Asp His His Gln Pro Gly Thr Gly Arg Tyr Gln Val Leu Leu Asn

Glu Glu Asp Asn Ser Glu Ser Ser Ala IIe Glu Gln Pro Pro Thr Ser

Asn Pro Ala Pro Gln Ile Val Gln Ala Val Ser Ser Ala Pro Ala Leu 35 40 45

Glu Thr Asp Ser Ser Pro Pro Pro Tyr Ser Ser lle Thr Val Glu Val 50 55 60

Pro Thr Thr Ser Asp Thr Glu Val Tyr Gly Glu Phe Tyr Pro Val Pro 65 70 75 80

Pro Pro Tyr Ser Val Ala Thr Ser Leu Pro Thr Tyr Asp Glu Ala Glu 85 90 95

Lys Ala Lys Ala Ala Ala Met Ala Ala Ala Ala Ala Glu Thr Ser Gln 100 105 110

Arg Ile Gin Giu Giu Cys Pro Pro Arg Asp Asp Phe Ser Asp Ala 115 120 125

Asp Gln Leu Arg Val Gly Asn Asp Gly Ile Phe Met Leu Ala Phe Phe 130 135 140

Met Ala Phe lle Phe Asn Trp Leu Gly Phe Cys Leu Ser Phe Cys lle 145 150 155 160

Thr Asn Thr lie Ala Gly Arg Tyr Gly Ala lie Cys Gly Phe Gly Leu 165 170 175

Ser Leu lle Lys Trp lle Leu lle Val Arg Phe Ser Asp Tyr Phe Thr 180 185 190

Gly Tyr Phe Asn Gly Gln Tyr Trp Leu Trp Trp Ile Phe Leu Val Leu 195 200 205

Gly Leu Leu Phe Phe Arg Gly Phe Val Asn Tyr Leu Lys Val Arg 210 215 220

Asn Met Ser Glu Ser Met Ala Ala Ala His Arg Thr Arg Tyr Phe Phe 225 230 235 240

Leu Leu

<210> 16

<211> 2324

<212> DNA

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<220>

<221> CDS

<222> (13).. (738)

<400> 16

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|                   |                   |                  |                   |                   |                   |                    |                  |                   | tca<br>Ser        |                   |                   |                  |                   |                   |                   | 99  |
|-------------------|-------------------|------------------|-------------------|-------------------|-------------------|--------------------|------------------|-------------------|-------------------|-------------------|-------------------|------------------|-------------------|-------------------|-------------------|-----|
|                   |                   |                  |                   |                   |                   |                    |                  |                   | gtg<br>Val        |                   |                   |                  |                   |                   |                   | 147 |
|                   |                   |                  |                   |                   |                   |                    |                  |                   | cca<br>Pro<br>55  |                   |                   |                  |                   |                   |                   | 195 |
| gtg<br>Val        | gaa<br>Glu        | gta<br>Val       | cct<br>Pro<br>65  | aca<br>Thr        | act<br>Thr        | tca<br>Ser         | gat<br>Asp       | aca<br>Thr<br>70  | gaa<br>Glu        | gtt<br>Val        | tac<br>Tyr        | ggt<br>Gly       | gag<br>Glu<br>75  | ttt<br>Phe        | tat<br>Tyr        | 243 |
| ccc<br>Pro        | gtg<br>Val        | cca<br>Pro<br>80 | cct<br>Pro        | ccc<br>Pro        | tat<br>Tyr        | agc<br>Ser         | gtt<br>Val<br>85 | gct<br>Ala        | acc<br>Thr        | tct<br>Ser        | ctt<br>Leu        | cct<br>Pro<br>90 | aca<br>Thr        | tac<br>Tyr        | gat<br>Asp        | 291 |
| gaa<br>Glu        | gct<br>Ala<br>95  | gag<br>Glu       | aag<br>Lys        | gct<br>Ala        | aaa<br>Lys        | gct<br>Ala<br>100  | gct<br>Ala       | gca<br>Ala        | atg<br>Met        | gca<br>Ala        | gct<br>Ala<br>105 | gca<br>Ala       | gca<br>Ala        | gca<br>Ala        | gaa<br>Glu        | 339 |
| aca<br>Thr<br>110 | tct<br>Ser        | caa<br>Gln       | aga<br>Arg        | att<br>He         | cag<br>Gln<br>115 | gag<br>Glu         | gaa<br>Glu       | gag<br>G u        | tgt<br>Cys        | cca<br>Pro<br>120 | cca<br>Pro        | aga<br>Arg       | gat<br>Asp        | gac<br>Asp        | ttc<br>Phe<br>125 | 387 |
| agt<br>Ser        | gat<br>Asp        | gca<br>Ala       | gac<br>Asp        | cag<br>Gln<br>130 | ctc<br>Leu        | aga<br>Arg         | gtg<br>Val       | ggg<br>Gly        | aat<br>Asn<br>135 | gat<br>Asp        | ggc<br>Gly        | att<br>lle       | ttc<br>Phe        | atg<br>Met<br>140 | ctg<br>Leu        | 435 |
| gca<br>Ala        | ttt<br>Phe        | ttc<br>Phe       | atg<br>Met<br>145 | gca<br>Ala        | ttt<br>Phe        | att<br>Ile         | ttc<br>Phe       | aac<br>Asn<br>150 | tgg<br>Trp        | ctt<br>Leu        | gga<br>Gly        | ttt<br>Phe       | tgt<br>Cys<br>155 | tta<br>Leu        | tcc<br>Ser        | 483 |
| Phe               | Cys               | He               | Thr               | Asn               | Thr               | lle                | Ala              | Gly               | agg<br>Arg        | Tyr               | Gly               | Ala              | Пe                | tgc<br>Cys        | gga<br>Gly        | 531 |
| ttt<br>Phe        | ggc<br>Gly<br>175 | ctt<br>Leu       | tcc<br>Ser        | ttg<br>Leu        | atc<br>lle        | aaa<br>Lys<br>180  | tgg<br>Trp       | atc<br>Ile        | ctt<br>Leu        | att<br>Ile        | gtc<br>Val<br>185 | agg<br>Arg       | ttt<br>Phe        | tct<br>Ser        | gat<br>Asp        | 579 |
| tat<br>Tyr<br>190 | ttt<br>Phe        | act<br>Thr       | gga<br>Gly        | tat<br>Tyr        | ttc<br>Phe<br>195 | aat<br>Asn         | gga<br>Gly       | cag<br>Gln        | tat<br>Tyr        | tgg<br>Trp<br>200 | ctt<br>Leu        | tgg<br>Trp       | tgg<br>Trp        | ata<br>He         | ttt<br>Phe<br>205 | 627 |
| ctt<br>Leu        | gta<br>Val        | ctt<br>Leu       | ggc<br>Gly        | ctg<br>Leu<br>210 | ctc<br>Leu        | ctt<br>Leu         | ttc<br>Phe       | ttc<br>Phe        | aga<br>Arg<br>215 | gga<br>Gly        | ttt<br>Phe        | gtt<br>Val       | aat<br>Asn        | tat<br>Tyr<br>220 | cta<br>Leu        | 675 |
| aaa<br>Lys        | gtc<br>Val        | aga<br>Arg       | aac<br>Asn<br>225 | atg<br>Met        | tct<br>Ser        | g <b>aa</b><br>Glu | agt<br>Ser       | atg<br>Met<br>230 | gca<br>Ala        | gct<br>Ala        | gct<br>Ala        | cat<br>His       | aga<br>Arg<br>235 | aca<br>Thr        | agg<br>Arg        | 723 |

778

tat ttc ttc tta ttg tagagactgc atcaacccga cattcctttc ttataccaat Tyr Phe Phe Leu Leu 240

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Leu Asn Ser Ala Arg Gly Ala Pro Glu Leu Leu Arg Gly Thr Ala Thr 20 25 30

Asn Ala Glu Val Ser Ala Ala Ala Ala Gly Ala Thr Gly Ser Glu Glu 35 40 45

Leu Pro Pro Gly Asp Arg Gly Cys Arg Asn Gly Gly Gly Arg Gly Pro 50 55 60

Ala Ala Thr Thr Ser Ser Thr Gly Val Ala Val Gly Ala Glu His Gly 65 70 75 80

Glu Asp Ser Leu Ser Arg Lys Pro Asp Pro Glu Pro Gly Arg Met Asp 85 90 95

His His Gln Pro Gly Thr Gly Arg Tyr Gln Val Leu Leu Asn Glu Glu 100 105 110

Asp Asn Ser Glu Ser Ser Ala IIe Glu Gln Pro Pro Thr Ser Asn Pro 115 120 125

Ala Pro Gln Ile Val Gln Ala Val Ser Ser Ala Pro Ala Leu Glu Thr 130 135 140

Asp Ser Ser Pro Pro Pro Tyr Ser Ser IIe Thr Val Glu Val Pro Thr 145 150 155 160

Thr Ser Asp Thr Glu Val Tyr Gly Glu Phe Tyr Pro Val Pro Pro Pro 165 170 175

Tyr Ser Val Ala Thr Ser Leu Pro Thr Tyr Asp Glu Ala Glu Lys Ala 180 185 190

Lys Ala Ala Ala Met Ala Ala Ala Ala Ala Glu Thr Ser Gln Arg Ile 195 200 205

Gln Glu Glu Cys Pro Pro Arg Asp Asp Phe Ser Asp Ala Asp Gln 210 215 220

Leu Arg Val Gly Asn Asp Gly Ile Phe Met Leu Ala Phe Phe Met Ala 225 230 235 240

Phe lle Phe Asn Trp Leu Gly Phe Cys Leu Ser Phe Cys lle Thr Asn 245 250 255

Thr lle Ala Gly Arg Tyr Gly Ala lle Cys Gly Phe Gly Leu Ser Leu 260 265 270

lle Lys Trp lle Leu lle Val Arg Phe Ser Asp Tyr Phe Thr Gly Tyr



| Phe          | Asn<br>290   | Gly        | GIn              | lyr              | lrp        | Leu<br>295       | Irp        | lrp              | He               | Phe        | 300              | Val        | Leu              | ч                | Leu                   |     |
|--------------|--|------------|------------------|------------------|------------|------------------|------------|------------------|------------------|------------|------------------|------------|------------------|------------------|-----------------------|-----|
| Leu<br>305   | Leu  | Phe        | Phe              | Arg              | Gly<br>310 | Phe              | Val        | Asn              | Tyr              | Leu<br>315 | Lys              | Val        | Arg              | Asn              | Met<br>320            |     |
| Ser          | Glu  | Ser        | Met              | Ala<br>325       | Ala        | Ala              | His        | Arg              | Thr<br>330       | Arg        | Tyr              | Phe        | Phe              | Leu<br>335       | Leu                   |     |
| <211<br><212 | <210> 18<br><211> 2636<br><212> DNA<br><213> Homo sapiens<br><220> |            |                  |                  |            |                  |            |                  |                  |            |                  |            |                  |                  |                       |     |
| <221         | )><br> > CE<br>2> (5   |            | (106             | 60)              |            |                  |            |                  |                  |            |                  |            |                  |                  |                       |     |
|              | )> 18<br>acttt   |            | catc             | tcct             | CC CA      | accca            | agcta      | a tad            | cct              | ссса       | ctgg             | gcggo      | ege į            |                  | tg gca<br>et Ala<br>1 | 58  |
|              | cgg<br>Arg   |            |                  |                  |            |                  |            |                  |                  |            |                  |            |                  |                  |                       | 106 |
| agc<br>Ser   | gcg<br>Ala<br>20   | cgc<br>Arg | ggc<br>Gly       | gcc<br>Ala       | ccg<br>Pro | gag<br>Glu<br>25 | ctt<br>Leu | ctc<br>Leu       | cgc<br>Arg       | gga<br>Gly | acc<br>Thr<br>30 | gcg<br>Ala | acc<br>Thr       | aac<br>Asn       | gcg<br>Ala            | 154 |
|              | gtc<br>Val   |            |                  |                  |            |                  |            |                  |                  |            |                  |            |                  |                  |                       | 202 |
| ccg<br>Pro   | gga<br>Gly   | gac<br>Asp | cgc<br>Arg       | ggc<br>Gly<br>55 | tgc<br>Cys | agg<br>Arg       | aac<br>Asn | gga<br>Gly       | ggc<br>Gly<br>60 | gga<br>Gly | agg<br>Arg       | ggc<br>Gly | cct<br>Pro       | gcg<br>Ala<br>65 | gcg<br>Ala            | 250 |
| acg<br>Thr   | acg<br>Thr   | tcg<br>Ser | tcg<br>Ser<br>70 | acg<br>Thr       | ggg<br>Gly | gtg<br>Val       | gcc<br>Ala | gtg<br>Val<br>75 | gga<br>Gly       | gct<br>Ala | gag<br>Glu       | cac<br>His | gga<br>Gly<br>80 | gaa<br>Glu       | gac<br>Asp            | 298 |
|              | ctc<br>Leu   |            |                  |                  |            |                  |            |                  |                  |            |                  |            |                  |                  |                       | 346 |
|              | ccg<br>Pro<br>100  |            |                  |                  |            |                  |            |                  |                  |            |                  |            |                  |                  |                       | 394 |
|              | gaa<br>Glu   |            |                  |                  |            |                  |            |                  |                  |            |                  |            |                  |                  |                       | 442 |

|                                   |                                   | tct tca gca<br>Ser Ser Ala        |                           |                                 |                                 | 490  |
|-----------------------------------|-----------------------------------|-----------------------------------|---------------------------|---------------------------------|---------------------------------|------|
| tcc cct cca<br>Ser Pro Pro        | cca tat agt<br>Pro Tyr Ser<br>150 | agt att act<br>Ser lle Thr<br>155 | Val Glu                   | Val Pro T                       | ca act tca<br>hr Thr Ser<br>60  | 538  |
| gat aca gaa<br>Asp Thr Glu<br>165 | gtt tac ggt<br>Val Tyr Gly        | gag ttt tat<br>Glu Phe Tyr<br>170 | ccc gtg<br>Pro Val        | cca cct c<br>Pro Pro P<br>175   | cc tat agc<br>ro Tyr Ser        | 586  |
| gtt gct acc<br>Val Ala Thr<br>180 | tct ctt cct<br>Ser Leu Pro        | aca tac gat<br>Thr Tyr Asp<br>185 | gaa gct<br>Glu Ala        | gag aag g<br>Glu Lys A<br>190   | ct aaa gct<br>Ia Lys Ala        | 634  |
| gct gca atg<br>Ala Ala Met<br>195 | gca gct gca<br>Ala Ala Ala<br>200 | gca gca gaa<br>Ala Ala Glu        | aca tct<br>Thr Ser<br>205 | caa aga a<br>Gln Arg l          | tt cag gag<br>le Gln Glu<br>210 | 682  |
| gaa gag tgt<br>Glu Glu Cys        | cca cca aga<br>Pro Pro Arg<br>215 | gat gac ttc<br>Asp Asp Phe        | agt gat<br>Ser Asp<br>220 | gca gac ca<br>Ala Asp G         | ag ctc aga<br>In Leu Arg<br>225 | 730  |
| gtg ggg aat<br>Val Gly Asn        | gat ggc att<br>Asp Gly lle<br>230 | ttc atg ctg<br>Phe Met Leu<br>235 | gca ttt<br>Ala Phe        | ttc atg go<br>Phe Met A<br>24   | la Phe lle                      | 778  |
| ttc aac tgg<br>Phe Asn Trp<br>245 | ctt gga ttt<br>Leu Gly Phe        | tgt tta tcc<br>Cys Leu Ser<br>250 | ttc tgt<br>Phe Cys        | atc acc aa<br>lle Thr As<br>255 | at acc ata<br>sn Thr lle        | 826  |
| gct gga agg<br>Ala Gly Arg<br>260 | tat ggt gct<br>Tyr Gly Ala        | atc tgc gga<br>lle Cys Gly<br>265 | Phe Gly                   | ctt tcc tt<br>Leu Ser Le<br>270 | eg atc aaa<br>eu lle Lys        | 874  |
| tgg atc ctt<br>Trp IIe Leu<br>275 | att gtc agg<br>ile Val Arg<br>280 | ttt tct gat<br>Phe Ser Asp        | tat ttt<br>Tyr Phe<br>285 | act gga ta<br>Thr Gly Ty        | at ttc aat<br>or Phe Asn<br>290 | 922  |
| gga cag tat<br>Gly Gln Tyr        | tgg ctt tgg<br>Trp Leu Trp<br>295 | tgg ata ttt<br>Trp lle Phe        | ctt gta<br>Leu Val<br>300 | ctt ggc ct<br>Leu Gly Le        | g ctc ctt<br>u Leu Leu<br>305   | 970  |
| Phe Phe Arg                       | gga ttt gtt<br>Gly Phe Val<br>310 | aat tat cta<br>Asn Tyr Leu<br>315 | aaa gtc<br>Lys Val        | aga aac at<br>Arg Asn Me<br>32  | et Ser Glu                      | 1018 |
|                                   |                                   | aga aca agg<br>Arg Thr Arg<br>330 |                           |                                 |                                 | 1060 |
| tagagactgc a                      | tcaacccga ca                      | attcctttc tta                     | taccaat                   | gtgaaatttc                      | cagatcatct                      | 1120 |
| gtaaacctac a                      | actttaata ga                      | agactact aat                      | aacagaa                   | gacaaattag                      | tgaagaaaag                      | 1180 |
| acggagtttc g                      | aaattgaat gg                      | cagggtgg ttt                      | ttgctta                   | caagccattt                      | ctgttcattc                      | 1240 |

tttaagtatc tatatttc ttgttttgca catatgcata tgtgcccat aagatattt 1300 gcatatactt gatagaaacc ataaagttgt agcagttaag tccagtcaca tttggttaat 1360 cagtgtttga tataattgaa agagttgagt ggataaacag tcttccagct tgtaaatgcc 1420 attgacttct gacctgacat ttagtataat aaaaatgaaa ttcttaacca tgtcaaatga 1480 tttagtttct ggctcttaga ctcatctggc agttctacac atgaaacatc ttttgttata 1540 taaggtgtat tgaaacctgc agtgctgatt attagaaagg atttgtcaga tttttgaaca 1600 tgatatttac attattatt aggaaaactc ttcctgtaaa taaccatgca taacttactt 1660 tctgcaatgt tttcttagaa attgtgtcca gatagctttc actaatttta aattaagtga 1720 actaaatata tatgtgtata tgtatacaca tatatataca cacacacata tatatattta 1780 gaaacgtgag tgttaaagat agaatttgtt ttaggacaaa ttttaagaaa atgtgggaat 1840 accaaatgtc ctttataaga aaaataaatt ttgttttaag ggacatacca gttttaggga 1900 ttttcagatg ggaagctgca tttttaggat tgcccatctt aagagatctt gcaggaagag 1960 attgtattag atattatatt tatttcattt aagataattt tcaaagttaa ttttctaaat 2020 aagataatto toatttgtgt ttgtotttta aaaggocaat aaaatatott toagtatoat 2080 tgtaataatt ttttagagtt taatttgtaa agcttagcaa ataaaatctt gtactatgaa 2140 tagcttcttg ctttatgact ttaggattaa cttgtaaaaa acatatcctg aactgagata 2200 tgcaaaatac tcattttcaa gttatggaaa tgtgtttgtg gcatatagga ctgtggggtc 2260 actactatat ttcccatctt gcaaatcatt ttatgtctca tctgtttttc ctttcggtta 2380 tatctttggt tttgaatacc aacatttaaa atgatggtat tttatctttt aaacttaaaa 2440 attatttaat acagctatat ggaccttata aaattgattt cttatttatt attagacatt 2500 actactaaaa ggtacatcta actattcagg gacatttttc catttccaaa aaataaaatt 2560 tattatgctt tataacctct tctgtatttt ctaatttttt cattgtcttt gataaataaa 2620 2636 acagttttgt tttgct

<sup>&</sup>lt;210> 19

<sup>&</sup>lt;211> 336

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

<sup>&</sup>lt;400> 19

Met Ala Arg Arg Ser Gln Arg Val Cys Ala Ser Gly Pro Ser Met

1 5 10 15

| Leu        | Asn        | Ser        | Ala<br>20  | Arg        | y          | Ala        | Pro        | Glu<br>25  | Leu        | Leu               | Arg        | Gly        | 30         | Ala        | Thr        |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|------------|
| Asn        | Ala        | Glu<br>35  | Val        | Ser        | Ala        | Ala        | Ala<br>40  | Ala        | Gly        | Ala               | Thr        | Gly<br>45  | Ser        | Glu        | Glu        |
| Leu        | Pro<br>50  | Pro        | Gly        | Asp        | Arg        | Gly<br>55  | Cys        | Arg        | Asn        | Gly               | Gly<br>60  | Gly        | Arg        | Gly        | Pro        |
| Ala<br>65  | Ala        | Thr        | Thr        | Ser        | Ser<br>70  | Thr        | Gly        | Val        | Ala        | <b>Va</b> l<br>75 | Gly        | Ala        | Glu        | His        | Gly<br>80  |
| Glu        | Asp        | Ser        | Leu        | Ser<br>85  | Arg        | Lys        | Pro        | Asp        | Pro<br>90  | Glu               | Pro        | Gly        | Arg        | Met<br>95  | Asp        |
| His        | His        | Gln        | Pro<br>100 | Gly        | Thr        | Gly        | Arg        | Tyr<br>105 | Gln        | Val               | Leu        | Leu        | Asn<br>110 | Glu        | Glu        |
| Asp        | Asn        | Ser<br>115 | Glu        | Ser        | Ser        | Ala        | 11e<br>120 | Glu        | Gln        | Pro               | Pro        | Thr<br>125 | Ser        | Asn        | Pro        |
| Ala        | Pro<br>130 | Gln        | lle        | Val        | GIn        | Ala<br>135 | Ala        | Ser        | Ser        | Ala               | Pro<br>140 | Ala        | Leu        | Glu        | Thr        |
| Asp<br>145 | Ser        | Ser        | Pro        | Pro        | Pro<br>150 | Tyr        | Ser        | Ser        | lle        | Thr<br>155        | Val        | Glu        | Val        | Pro        | Thr<br>160 |
| Thr        | Ser        | Asp        | Thr        | Glu<br>165 | Val        | Tyr        | Gly        | Glu        | Phe<br>170 | Tyr               | Pro        | Val        | Pro        | Pro<br>175 | Pro        |
| Tyr        | Ser        | Val        | Ala<br>180 |            | Ser        | Leu        | Pro        | Thr<br>185 | Tyr        | Asp               | Glu        | Ala        | G1u<br>190 | Lys        | Ala        |
| Lys        | Ala        | Ala<br>195 | Ala        | Met        | Ala        | Ala        | Ala<br>200 | Ala        | Ala        | Glu               | Thr        | Ser<br>205 | Gln        | Arg        | lle        |
| Gln        | Glu<br>210 | Glu        | Glu        | Cys        | Pro        | Pro<br>215 | Arg        | Asp        | Asp        | Phe               | Ser<br>220 | Asp        | Ala        | Asp        | Gln        |
| Leu<br>225 | Arg        | Val        | Gly        | Asn        | Asp<br>230 | Gly        | He         | Phe        | Met        | Leu<br>235        | Ala        | Phe        | Phe        | Met        | Ala<br>240 |
| Phe        | lle        | Phe        | Asn        | Trp<br>245 | Leu        | Gly        | Phe        | Cys        | Leu<br>250 | Ser               | Phe        | Cys        | lle        | Thr<br>255 | Asn        |
| Thr        | He         | Ala        | Gly<br>260 | Arg        | Tyr        | Gly        | Ala        | 11e<br>265 | Cys        | Gly               | Phe        | Gly        | Leu<br>270 | Ser        | Leu        |
| lle        | Lys        | Trp<br>275 | lle        | Leu        | He         | Val        | Arg<br>280 | Phe        | Ser        | Asp               | Tyr        | Phe<br>285 | Thr        | Gly        | Tyr        |
| Phe        | Asn<br>290 | Gly        | Gln        | Tyr        | Trp        | Leu<br>295 | Trp        | Trp        | He         | Phe               | Leu<br>300 | Val        | Leu        | Gly        | Leu        |
| Leu<br>305 | Leu        | Phe        | Phe        | Arg        | Gly<br>310 | Phe        | Val        | Asn        | Tyr        | Leu<br>315        | Lys        | Val        | Arg        | Asn        | Met<br>320 |
| Ser        | Glu        | Ser        | Met        | Ala        | Ala        | Ala        | His        | Arø        | Thr        | Arø               | Tvr        | Phe        | Phe        | Leu        | Leu        |

| <21<br><21        | <210> 20<br><211> 2636<br><212> DNA<br><213> Homo sapiens   |                  |                   |                   |                   |                   |                  |                   |                    |                   |                   |                  |                   |                   |                       |     |
|-------------------|---|------------------|-------------------|-------------------|-------------------|-------------------|------------------|-------------------|--------------------|-------------------|-------------------|------------------|-------------------|-------------------|-----------------------|-----|
| <22<br><22        | <220> <221> CDS <222> (53)(1060)  <400> 20 cttacttttc catctcctcc cacccagcta taccctccca ctggcggcgc gg atg gca 58 |                  |                   |                   |                   |                   |                  |                   |                    |                   |                   |                  |                   |                   |                       |     |
|                   |   |                  | cato              | tcct              | сс с              | accc              | agct             | a ta              | ccct               | ссса              | ctg               | gcgg             | cgc               |                   | tg gca<br>et Ala<br>1 |     |
| cgc<br>Arg        | cgg<br>Arg  | cgg<br>Arg<br>5  | Ser               | cag<br>G n        | cga<br>Arg        | gtc<br>Val        | tgc<br>Cys<br>10 | Ala               | agc<br>Ser         | ggt<br>Gly        | ccg<br>Pro        | agc<br>Ser<br>15 | atg<br>Met        | ctc<br>Leu        | aat<br>Asn            | 106 |
| agc<br>Ser        | gcg<br>Ala<br>20  | Arg              | ggc<br>Gly        | gcc<br>Ala        | ccg<br>Pro        | gag<br>Glu<br>25  | ctt<br>Leu       | ctc<br>Leu        | cgc<br>Arg         | gga<br>Gly        | acc<br>Thr<br>30  | gcg<br>Ala       | acc<br>Thr        | aac<br>Asn        | gcg<br>Ala            | 154 |
| gag<br>Glu<br>35  | Val   | tcg<br>Ser       | gcg<br>Ala        | gcc<br>Ala        | gct<br>Ala<br>40  | gcg<br>Ala        | gga<br>Gly       | gcc<br>Ala        | aca<br>Thr         | gga<br>Gly<br>45  | agt<br>Ser        | gaa<br>Glu       | gag<br>Glu        | ctt<br>Leu        | ccg<br>Pro<br>50      | 202 |
| ccg<br>Pro        | gga<br>Gly  | gac<br>Asp       | Arg               | ggc<br>Gly<br>55  | tgc<br>Cys        | agg<br>Arg        | aac<br>Asn       | gga<br>Gly        | ggc<br>Gly<br>60   | gga<br>Gly        | agg<br>Arg        | ggc<br>Gly       | cct<br>Pro        | gcg<br>Ala<br>65  | gcg<br>Ala            | 250 |
| acg<br>Thr        | acg<br>Thr  | tcg<br>Ser       | tcg<br>Ser<br>70  | acg<br>Thr        | ggg<br>Gly        | gtg<br>Val        | gcc<br>Ala       | gtg<br>Val<br>75  | gga<br>Gly         | gct<br>Ala        | gag<br>Glu        | cac<br>His       | gga<br>Gly<br>80  | gaa<br>Glu        | gac<br>Asp            | 298 |
| tcc<br>Ser        | ctc<br>Leu  | tct<br>Ser<br>85 | cgg<br>Arg        | aag<br>Lys        | ccg<br>Pro        | gat<br>Asp        | ccc<br>Pro<br>90 | gag<br>Glu        | ccg<br>Pro         | ggc<br>Gly        | agg<br>Arg        | atg<br>Met<br>95 | gat<br>Asp        | cac<br>His        | cac<br>His            | 346 |
| cag<br>Gln        | ccg<br>Pro<br>100   | ggg<br>Gly       | act<br>Thr        | ggg<br>Gly        | cgc<br>Arg        | tac<br>Tyr<br>105 | cag<br>Gln       | gtg<br>Val        | ctt<br>Leu         | ctt<br>Leu        | aat<br>Asn<br>110 | gaa<br>Glu       | gag<br>Glu        | gat<br>Asp        | aac<br>Asn            | 394 |
| tca<br>Ser<br>115 | gaa<br>Glu  | tca<br>Ser       | tcg<br>Ser        | gct<br>Ala        | ata<br>  e<br>120 | gag<br>Glu        | cag<br>Gln       | cca<br>Pro        | cct<br>Pro         | act<br>Thr<br>125 | tca<br>Ser        | aac<br>Asn       | cca<br>Pro        | gca<br>Ala        | ccg<br>Pro<br>130     | 442 |
| cag<br>Gln        | att<br>  e  | gtg<br>Val       | cag<br>Gln        | gct<br>Ala<br>135 | gcg<br>Ala        | tct<br>Ser        | tca<br>Ser       | Ala               | cca<br>Pro<br>140  | gca<br>Ala        | ctt<br>Leu        | gaa<br>Glu       | act<br>Thr        | gac<br>Asp<br>145 | tct<br>Ser            | 490 |
| tcc<br>Ser        | cct<br>Pro  | cca<br>Pro       | cca<br>Pro<br>150 | tat<br>Tyr        | agt<br>Ser        | agt<br>Ser        | att<br>Ile       | act<br>Thr<br>155 | gtg<br><b>Va</b> l | gaa<br>Glu        | gta<br>Val        | cct<br>Pro       | aca<br>Thr<br>160 | act<br>Thr        | tca<br>Ser            | 538 |

gat aca gaa gtt tac ggt gag ttt tat ccc gtg cca cct ccc tat agc  $\phantom{0}586$ 

| Asp Thr Glu Val Tyr y Glu Phe Tyr Pro Val Pro Pro Tyr Ser<br>165 170 175   |   |
|--|---|
| gtt gct acc tct ctt cct aca tac gat gaa gct gag aag gct aaa gct 634<br>Val Ala Thr Ser Leu Pro Thr Tyr Asp Glu Ala Glu Lys Ala Lys Ala<br>180 185 190  |   |
| gct gca atg gca gct gca gca gca gaa aca tct caa aga att cag gag Ala Ala Met Ala Ala Ala Ala Glu Thr Ser Gln Arg lle Gln Glu 195 200 205 210            |   |
| gaa gag tgt cca cca aga gat gac ttc agt gat gca gac cag ctc aga Glu Glu Cys Pro Pro Arg Asp Asp Phe Ser Asp Ala Asp Gln Leu Arg 215 220 225            |   |
| gtg ggg aat gat ggc att ttc atg ctg gca ttt ttc atg gca ttt att 778<br>Val Gly Asn Asp Gly Ile Phe Met Leu Ala Phe Phe Met Ala Phe Ile<br>230 235 240  |   |
| ttc aac tgg ctt gga ttt tgt tta tcc ttc tgt atc acc aat acc ata Phe Asn Trp Leu Gly Phe Cys Leu Ser Phe Cys Ile Thr Asn Thr Ile 245 250 255            |   |
| gct gga agg tat ggt gct atc tgc gga ttt ggc ctt tcc ttg atc aaa 874<br>Ala Gly Arg Tyr Gly Ala lle Cys Gly Phe Gly Leu Ser Leu lle Lys<br>260 265 270  |   |
| tgg atc ctt att gtc agg ttt tct gat tat ttt act gga tat ttc aat Trp Ile Leu Ile Val Arg Phe Ser Asp Tyr Phe Thr Gly Tyr Phe Asn 275 280 285 290        | - |
| gga cag tat tgg ctt tgg tgg ata ttt ctt gta ctt ggc ctg ctc ctt 970<br>Gly Gln Tyr Trp Leu Trp Trp lle Phe Leu Val Leu Gly Leu Leu Leu<br>295 300 305  |   |
| ttc ttc aga gga ttt gtt aat tat cta aaa gtc aga aac atg tct gaa 1018<br>Phe Phe Arg Gly Phe Val Asn Tyr Leu Lys Val Arg Asn Met Ser Glu<br>310 315 320 |   |
| agt atg gca gct gct cat aga aca agg tat ttc ttc tta ttg  Ser Met Ala Ala Ala His Arg Thr Arg Tyr Phe Phe Leu Leu  325  330  335                        |   |
| tagagactgc atcaacccga cattcctttc ttataccaat gtgaaatttc cagatcatct 1120   |   |
| gtaaacctac aactttaata gaagactact aataacagaa gacaaattag tgaagaaaag 1180   |   |
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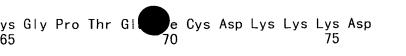
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Ser Arg lie Trp Pro Lys Lys Ala IIe Gin Glu Ser Asn Asp Thr Asn 35 40 45

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Pro Leu Phe Gly lle Met Ser Ser Asp Ser Ala Asp Pro Phe Tyr Trp 50 55 60

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Met Ala Ile Lys Phe Leu Glu Val Ile Lys Pro Phe Cys Val Ile

1 5 10 15

ctg ccg gaa att cag aag cca gag agg aag att cag ttt aag gag aaa 157 Leu Pro Glu Ile Gln Lys Pro Glu Arg Lys Ile Gln Phe Lys Glu Lys 20 25 30

gtg ctg tgg acc gct atc acc ctc ttt atc ttc tta gtg tgc tgc cag 205 Val Leu Trp Thr Ala lle Thr Leu Phe lle Phe Leu Val Cys Cys Gln 35 40 45

| att<br>Ile | ccc<br>Pro | ctg<br>Leu<br>50 | ttt<br>Phe | ggg<br>Gly | lle | atg<br>Met | tct<br>Ser<br>55 | tca<br>Ser | gat<br>Asp | tca<br>Ser | gct<br>Ala | gac<br>Asp<br>60 | c<br>Pro | ttc<br>Phe | tat<br>Tyr | 253 |
|------------|------------|------------------|------------|------------|-----|------------|------------------|------------|------------|------------|------------|------------------|----------|------------|------------|-----|
|------------|------------|------------------|------------|------------|-----|------------|------------------|------------|------------|------------|------------|------------------|----------|------------|------------|-----|

tgg atg aga gtg att cta gcc tct aac aga ggc aca ttg atg gag cac 301 Trp Met Arg Val IIe Leu Ala Ser Asn Arg Gly Thr Leu Met Glu His 65 70 75

tct ctc tct ggc ctt tagggagtcc cctcttagga caggcactgc ccagcagcaa 356 Ser Leu Ser Gly Leu 80

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Leu Trp Thr Ala IIe Thr Leu Phe IIe Phe Leu Val Cys Cys Gln IIe 35 40 45

Pro Leu Phe Gly IIe Met Ser Ser Asp Ser Ala Asp Pro Val His Ala 50 55 60

Val Val Tyr IIe Val Phe Met Leu Gly Ser Cys Ala Phe Phe Ser Lys 65 70 75 80

Thr Trp lle Glu Val Ser Gly Ser Ser Ala Lys Asp Val Ala Lys Gln 85 90 95

Leu Lys Glu Gln Gln Met Val Met Arg Gly His Arg Glu Thr Ser Met 100 105 110

Val His Glu Leu Asn Arg Tyr lle Pro Thr Ala Ala Ala Phe Gly Gly 115 120 125

Leu Cys Ile Gly Ala Leu Ser Val Leu Ala Asp Phe Leu Gly Ala Ile 130 135 140

Gly Ser Gly Thr Gly IIe Leu Leu Ala Val Thr IIe IIe Tyr Gln Tyr 145 150 155 160

Phe Glu lle Phe Val Lys Glu Gln Ser Glu Val Gly Ser Met Gly Ala 165 170 175

Leu Leu Phe

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<400> 26

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Met

1

gca atc aaa ttt ctg gaa gtc atc aag ccc ttc tgt gtc atc ctg ccg Ala lie Lys Phe Leu Glu Val lie Lys Pro Phe Cys Val lie Leu Pro

| gaa att cag aag cca gag agg aag att cag ttt aag gag aaa gtg ctg 212<br>Glu lle Gln Lys Pro Glu Arg Lys Ile Gln Phe Lys Glu Lys Val Leu<br>20 25 30    |
|---|
| tgg acc gct atc acc ctc ttt atc ttc tta gtg tgc tgc cag att ccc 260 Trp Thr Ala lle Thr Leu Phe lle Phe Leu Val Cys Cys Gin lle Pro 35 40 45          |
| ctg ttt ggg atc atg tct tca gat tca gct gac ccg gtc cat gca gtt 308<br>Leu Phe Gly lle Met Ser Ser Asp Ser Ala Asp Pro Val His Ala Val<br>50 55 60 65 |
| gta tac ata gtg ttc atg ctg ggc tcc tgt gca ttc ttc tcc aaa acg 356<br>Val Tyr lle Val Phe Met Leu Gly Ser Cys Ala Phe Phe Ser Lys Thr<br>70 75 80    |
| tgg att gag gtc tca ggt tcc tct gcc aaa gat gtt gca aag cag ctg 404<br>Trp lle Glu Val Ser Gly Ser Ser Ala Lys Asp Val Ala Lys Gln Leu<br>85 90 95    |
| aag gag cag cag atg gtg atg aga ggc cac cga gag acc tcc atg gtc  Lys Glu Gln Met Val Met Arg Gly His Arg Glu Thr Ser Met Val  100 105 110             |
| cat gaa ctc aac cgg tac atc ccc aca gcc gcg gcc ttt ggt ggg ctg His Glu Leu Asn Arg Tyr lle Pro Thr Ala Ala Ala Phe Gly Gly Leu 115 120 125           |
| tgc atc ggg gcc ctc tcg gtc ctg gct gac ttc cta ggc gcc att ggg Cys lle Gly Ala Leu Ser Val Leu Ala Asp Phe Leu Gly Ala lle Gly 130 135 140 145       |
| tct gga acc ggg atc ctg ctc gca gtc aca atc atc tac cag tac ttt 596<br>Ser Gly Thr Gly IIe Leu Leu Ala Val Thr IIe IIe Tyr Gln Tyr Phe<br>150 155 160 |
| gag atc ttc gtt aag gag caa agc gag gtt ggc agc atg ggg gcc ctg<br>Glu lle Phe Val Lys Glu Gln Ser Glu Val Gly Ser Met Gly Ala Leu<br>165 170 175     |
| ctc ttc tgagcccgtc tcccggacag gttgaggaag ctgctccaga agcgcctcgg 700<br>Leu Phe   |
| aaggggagct ctcatcatgg cgcgtgctgc tgcggcatat ggactttaa taatgtttt 760   |
| gaatttegta ttetteatt eeactgtgta aagtgetaga eatttteeaa tttaaaattt 820  |
| tgctttttat cctggcactg gcaaaaagaa ctgtgaaagt gaatttattc agccgactgc 880   |
| cagagaagtg ggaatggtat aggattgtcc ccaagtgtcc atgtaacttt tgttttaacc 940   |
| tttgcacctt ctcagtgctg tatgcggctg cagccgtctc acctgtttcc ccacaaaggg 1000  |
| aatttctcac tctggttgga agcacaaaca ctgaaatgtc tacgtttcat tttggcagta 1060  |
| gggtgtgaag ctgggagcag atcatgtatt tcccggagac atgggacctt gctggcatgt 1120  |

tgttttcct tatttaaaa gtgattttt taaggacaga acttcttcca aagacaccat 1180
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<213> Homo sapiens

Pro Arg Ile Gin Gly Tyr Pro Leu Met Gly Ser Pro Leu Leu Met Thr 20 25 30

Ser lle Leu Leu Thr Tyr Val Tyr Phe Val Leu Ser Leu Gly Pro Arg 35 40 45

lle Met Ala Asn Arg Lys Pro Phe Gln Leu Arg Gly Phe Met lle Val 50 55 60

Tyr Asn Phe Ser Leu Val Ala Leu Ser Leu Tyr Ile Val Tyr Glu Phe 65 70 75 80

Leu Met Ser Gly Trp Leu Ser Thr Tyr Thr Trp Arg Cys Asp Pro Val 85 90 95

Asp Tyr Ser Asn Ser Pro Glu Ala Leu Arg Met Val Arg Val Ala Trp 100 105 110

Leu Phe Leu Phe Ser Lys Phe lle Glu Leu Met Asp Thr Val lle Phe 115 120 125

lle Leu Arg Lys Lys Asp Gly Gln Val Thr Phe Leu His Val Phe His 130 135 140

| His Ser Val Leu Pro Trp Ser Trp Trp Trp Gly Val Lys II<br>145 150 155  | e Ala Pro<br>160            |
|--|-----------------------------|
| Gly Gly Met Gly Ser Phe His Ala Met lle Asn Ser Ser Va<br>165 170  | l His Val<br>175            |
| lle Met Tyr Leu Tyr Tyr Gly Leu Ser Ala Phe Gly Pro Va<br>180 185 19   |                             |
| Pro Tyr Leu Trp Trp Lys Lys His Met Thr Ala lle Gln Le<br>195 200 205  | u lle Gin                   |
| Phe Val Leu Val Ser Leu His IIe Ser Gln Tyr Tyr Phe Me<br>210 215 220  | t Ser Ser                   |
| Cys Asn Tyr Gln Tyr Pro Val lle lle His Leu lle Trp Me<br>225 230 235  | t Tyr Gly<br>240            |
| Thr lie Phe Phe Met Leu Phe Ser Asn Phe Trp Tyr His Se<br>245 250  | r Tyr Thr<br>255            |
| Lys Gly Lys Arg Leu Pro Arg Ala Leu Gln Gln Asn Gly Al<br>260 265 27   |                             |
| lle Ala Lys <b>Vai</b> Lys Ala Asn<br>275  |                             |
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| tgctccctcc gagcgctccg ccgttgcccg cctggcccct acggagtcct   | tagccagg 118                |
| atg gag gct gtt gtg aac ttg tac caa gag gtg atg aag ca<br>Met Glu Ala Val Val Asn Leu Tyr Gln Glu Val Met Lys Hi<br>1 5 10   |                             |
| ccc cgg atc cag ggc tac cct ctg atg ggg tcc ccc ttg ct<br>Pro Arg lle Gln Gly Tyr Pro Leu Met Gly Ser Pro Leu Le<br>20 25 3  |                             |
| tcc att ctc ctg acc tac gtg tac ttc gtt ctc tca ctt gg<br>Ser lle Leu Leu Thr Tyr Val Tyr Phe Val Leu Ser Leu Gl<br>35 40 45 | g cct cgc 262<br>y Pro Arg  |
| atc atg gct aat cgg aag ccc ttc cag ctc cgt ggc ttc at<br>lle Met Ala Asn Arg Lys Pro Phe Gln Leu Arg Gly Phe Me<br>50 55 60 | g att gtc 310<br>et lle Val |

| tac<br>Tyr<br>65 | aac<br>Asn | ttc<br>Phe | tca<br>Ser        | ctg<br>Leu        | gtg<br>Val<br>70 | gca<br>Ala | ctc<br>Leu | tcc<br>Ser        | ctc<br>Leu        | tac<br>Tyr<br>75 | att<br>Ile        | gtc<br>Val | tat<br>Tyr        | gag<br>Glu        | ttc<br>Phe<br>80 | 358 |
|------------------|------------|------------|-------------------|-------------------|------------------|------------|------------|-------------------|-------------------|------------------|-------------------|------------|-------------------|-------------------|------------------|-----|
| ctg<br>Leu       | atg<br>Met | tcg<br>Ser | ggc<br>Gly        | tgg<br>Trp<br>85  | ctg<br>Leu       | agc<br>Ser | acc<br>Thr | tat<br>Tyr        | acc<br>Thr<br>90  | tgg<br>Trp       | cgc<br>Arg        | tgt<br>Cys | gac<br>Asp        | cct<br>Pro<br>95  | gtg<br>Val       | 406 |
|                  |            |            |                   |                   |                  |            |            |                   | agg<br>Arg        |                  |                   |            |                   |                   |                  | 454 |
|                  |            |            |                   |                   |                  |            |            |                   | ctg<br>Leu        |                  |                   |            |                   |                   |                  | 502 |
|                  |            |            |                   |                   |                  |            |            |                   | acc<br>Thr        |                  |                   |            |                   |                   |                  | 550 |
|                  |            |            |                   |                   |                  |            |            |                   | tgg<br>Trp        |                  |                   |            |                   |                   |                  | 598 |
|                  |            |            |                   |                   |                  |            |            |                   | ata<br>Ile<br>170 |                  |                   |            |                   |                   |                  | 646 |
| ata<br>Ile       | atg<br>Met | tac<br>Tyr | ctg<br>Leu<br>180 | Tyr               | tac<br>Tyr       | gga<br>Gly | tta<br>Leu | tct<br>Ser<br>185 | gcc<br>Ala        | ttt<br>Phe       | ggc<br>Gly        | cct<br>Pro | gtg<br>Val<br>190 | gca<br>Ala        | caa<br>Gln       | 694 |
|                  |            |            |                   |                   |                  |            |            |                   | aca<br>Thr        |                  |                   |            |                   |                   |                  | 742 |
| ttt<br>Phe       | Val        | Leu        | Val               | Ser               | ctg<br>Leu       | His        | lle        | Ser               | cag<br>Gln        | Tyr              | Tyr               | Phe        | atg<br>Met        | tcc<br>Ser        | agc<br>Ser       | 790 |
|                  |            |            |                   |                   |                  |            |            |                   | cac<br>His        |                  |                   |            |                   |                   |                  | 838 |
| acc<br>Thr       | atc<br>lle | ttc<br>Phe | ttc<br>Phe        | atg<br>Met<br>245 | ctg<br>Leu       | ttc<br>Phe | tcc<br>Ser | aac<br>Asn        | ttc<br>Phe<br>250 | tgg<br>Trp       | tat<br>Tyr        | cac<br>His | tct<br>Ser        | tat<br>Tyr<br>255 | acc<br>Thr       | 886 |
| aag<br>Lys       | ggc<br>Gly | aag<br>Lys | cgg<br>Arg<br>260 | ctg<br>Leu        | ccc<br>Pro       | cgt<br>Arg | gca<br>Ala | ctt<br>Leu<br>265 | cag<br>Gln        | caa<br>Gln       | aat<br>Asn        | gga<br>Gly | gct<br>Ala<br>270 | cca<br>Pro        | ggt<br>Gly       | 934 |
|                  |            |            |                   |                   | gcc<br>Ala       |            | tgaį       | gaago             | cat (             | ggcci            | taga <sup>.</sup> | ta gį      | gcgc              | ccaco             |                  | 985 |

taagtgcctc aggactgcac cttagggcag tgtccgtcag tgccctctcc acctacacct 1045

gtgaccaagg cttatgtgt caggactgag caggggactg gccctccct ccccacagct 1105 gctctacagg gaccacggct ttggttcctc acccacttcc cccgggcagc tccagggatg 1165 tggcctcatt gctgtctgcc actccagagc tgggggctaa aagggctgta cagttattc 1225 cccctccctg ccttaaaact tgggagagga gcactcaggg ctggccccac aaagggtctc 1285 gtggccttt tcctcacaca gaagaggtca gcaataatgt cactgtggac ccagtctcac 1345 tcctccaccc cacacactga agcagtagct tctgggccaa aggtcagggt gggcggggc 1405 ctgggaatac agcctgtgga ggctgcttac tcaacttgtg tcttaattaa aagtgacaga 1465 ggaaacc

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<211> 137

<212> PRT

<213> Homo sapiens

<400> 29

Met Gly Phe Gly Ala Thr Leu Ala Val Gly Leu Thr Ile Phe Val Leu 1 5 10 15

Ser Val Val Thr lie lie lie Cys Phe Thr Cys Ser Cys Cys Leu 20 25 30

Tyr Lys Thr Cys Arg Arg Pro Arg Pro Val Val Thr Thr Thr Ser 35 40 45

Thr Thr Val Val His Ala Pro Tyr Pro Gln Pro Pro Ser Val Pro Pro 50 55 60

Ser Tyr Pro Gly Pro Ser Tyr Gln Gly Tyr His Thr Met Pro Pro Gln 65 70 75 80

Pro Gly Met Pro Ala Ala Pro Tyr Pro Met Gln Tyr Pro Pro Pro Tyr 85 90 95

Pro Ala Gin Pro Met Gly Pro Pro Ala Tyr His Glu Thr Leu Ala Gly 100 105 110

Gly Ala Ala Ala Pro Tyr Pro Ala Ser Gln Pro Pro Tyr Asn Pro Ala 115 120 125

Tyr Met Asp Ala Pro Lys Ala Ala Leu 130 135

<210> 30

<211> 1788

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<400> 30

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<400> 31

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Ser Val Val Thr lle lle lle Cys Phe Thr Cys Ser Cys Cys Leu 20 25 30

Tyr Lys Thr Cys Arg Arg Pro Arg Pro Val Val Thr Thr Thr Ser 35 40 45

Thr Thr Val Val His Ala Pro Tyr Pro Gln Pro Pro Ser Val Pro Pro 50 55 60

Ser Tyr Pro Gly Pro Ser Tyr Gln Gly Tyr His Thr Met Pro Pro Gln 65 70 75 80

Pro Gly Met Pro Ala Ala Pro Tyr Pro Met Gln Tyr Pro Pro Pro Tyr 85 90 95

Pro Ala Gln Pro Met Gly Pro Pro Ala Tyr His Glu Thr Leu Ala Gly 100 105 110

Glu Cys Pro Cys Gln Leu 115

<sup>&</sup>lt;210> 31

<sup>&</sup>lt;211> 118

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

| <211<br><212     | > 32<br>> 19<br>> DN<br>> Ho | 80<br>A          | sapie            | ens              |                  |                  |                  |                  |                  |                  |                   |                  |                  |                  |                  |     |
|------------------|------------------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|-------------------|------------------|------------------|------------------|------------------|-----|
|                  | > CC                         |                  | (444             | 1)               |                  |                  |                  |                  |                  |                  |                   |                  |                  |                  |                  |     |
|                  | )> 32<br>(gagg               |                  | attga            | aact             | g ag             | gtggo            | ccac             | gat              | ggga             | aga              | gggg              | gaaag            | gcc (            | caggg            | ggtaca           | 60  |
| ggag             | gcct                         | ct g             | gggtg            | gaagg            | gc ag            | gaggo            | taad             | atg<br>Met       | t Gly            | g tto<br>/ Phe   | gga<br>Gly        | agce<br>Ala      | a Th             | c ttg<br>r Lei   | g gcc<br>ı Ala   | 114 |
| gtt<br>Val       | ggc<br>Gly<br>10             | ctg<br>Leu       | acc<br>Thr       | atc<br>Ile       | ttt<br>Phe       | gtg<br>Val<br>15 | ctg<br>Leu       | tct<br>Ser       | gtc<br>Val       | gtc<br>Val       | act<br>Thr<br>20  | atc<br>lle       | atc<br>He        | atc<br>lle       | tgc<br>Cys       | 162 |
| ttc<br>Phe<br>25 | acc<br>Thr                   | tgc<br>Cys       | tcc<br>Ser       | tgc<br>Cys       | tgc<br>Cys<br>30 | tgc<br>Cys       | ctt<br>Leu       | tac<br>Tyr       | aag<br>Lys       | acg<br>Thr<br>35 | tgc<br>Cys        | cgc<br>Arg       | cga<br>Arg       | cca<br>Pro       | cgt<br>Arg<br>40 | 210 |
| ccg<br>Pro       | gtt<br>Val                   | gtc<br>Val       | acc<br>Thr       | acc<br>Thr<br>45 | acc<br>Thr       | aca<br>Thr       | tcc<br>Ser       | acc<br>Thr       | act<br>Thr<br>50 | gtg<br>Val       | gtg<br>Val        | cat<br>His       | gcc<br>Ala       | cct<br>Pro<br>55 | tat<br>Tyr       | 258 |
| cct<br>Pro       | cag<br>G n                   | cct<br>Pro       | cca<br>Pro<br>60 | agt<br>Ser       | gtg<br>Val       | ccg<br>Pro       | ccc<br>Pro       | agc<br>Ser<br>65 | tac<br>Tyr       | cct<br>Pro       | gga<br>Gly        | cca<br>Pro       | agc<br>Ser<br>70 | tac<br>Tyr       | cag<br>G n       | 306 |
| ggc<br>Gly       | tac<br>Tyr                   | cac<br>His<br>75 | acc<br>Thr       | atg<br>Met       | ccg<br>Pro       | cct<br>Pro       | cag<br>Gln<br>80 | cca<br>Pro       | ggg<br>Gly       | atg<br>Met       | cca<br>Pro        | gca<br>Ala<br>85 | gca<br>Ala       | ccc<br>Pro       | tac<br>Tyr       | 354 |
| cca<br>Pro       | atg<br>Met<br>90             | cag<br>Gln       | tac<br>Tyr       | cca<br>Pro       | cca<br>Pro       | cct<br>Pro<br>95 | tac<br>Tyr       | cca<br>Pro       | gcc<br>Ala       | cag<br>Gln       | ccc<br>Pro<br>100 | atg<br>Met       | ggc<br>Gly       | cca<br>Pro       | ccg<br>Pro       | 402 |
|                  |                              |                  | gag<br>Glu       |                  |                  |                  |                  |                  |                  |                  |                   |                  |                  |                  |                  | 444 |
| tago             | ccct                         | gcc (            | cgac             | ttcc             | cg a             | gtct             | ctgc             | c ag             | catc             | cctc             | ggg               | cacc             | cat              | ccca             | aactac           | 504 |
| atca             | actca                        | aac a            | aggc             | ctct             | gc co            | cctt             | tctg             | c tt             | gcct             | gcca             | ctc               | acacı            | ggc              | agcc             | caccat           | 564 |
| gcto             | caca                         | gcc a            | аасса            | aggg             | tc c             | tctc             | tgct             | t tc             | agga             | ggag             | cag               | ccgc             | gcc              | ctac             | cccgcc           | 624 |
| agco             | cagc                         | ctc              | ctta             | caac             | cc g             | gcct             | acat             | g ga             | tgcc             | ccga             | agg               | cggc             | cct              | ctga             | gcattc           | 684 |
| cct              | ggcc <sup>-</sup>            | tct              | ctgg             | ctgc             | ca c             | ttgg             | ttat             | g tt             | gtgt             | gtgt             | gcg               | tgag             | tgg              | tgtg             | caggcg           | 744 |
| cgg.             | ttcc                         | tta              | cgcc             | ccat             | gt g             | tgct             | gtgt             | g tg             | tcca             | ggca             | cgg               | ttcc             | tta              | cgcc             | ccatgt           | 804 |

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Pro Pro Tyr Thr Asp Ala Pro Pro Ala Tyr Ser Glu Leu Tyr Arg Pro 35 40 45

Ser Phe Val His Pro Gly Ala Ala Thr Val Pro Thr Met Ser Ala Ala 50 55 60

Phe Pro Gly Ala Ser Leu Tyr Leu Pro Met Ala Gln Ser Val Ala Val

| Glv | Pro | Leu | Glv | Ser | Thr | He | Pro | Met | Ala | Tyr | Tyr | Pro | Val | Gly | Pro |
|-----|-----|-----|-----|-----|-----|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|     |     |     | •   | 85  |     |    |     |     | 90  |     |     |     |     | 95  |     |

lle Tyr Pro Pro Gly Ser Thr Val Leu Val Glu Gly Gly Tyr Asp Ala 100 105 110

Gly Ala Arg Phe Gly Ala Gly Ala Thr Ala Gly Asn Ile Pro Pro Pro 115 120 125

Pro Pro Gly Cys Pro Pro Asn Ala Ala Gln Leu Ala Val Met Gln Gly 130 135 140

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Ser Asp Gly Gly Tyr Thr lle Trp 165

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Met Asn Ser Lys Gly Gln Tyr Pro Thr Gln Pro Thr Tyr Pro

1 5 10

gtg cag cct cct ggg aat cca gta tac cct cag acc ttg cat ctt cct 159
Val Gln Pro Pro Gly Asn Pro Val Tyr Pro Gln Thr Leu His Leu Pro
15 20 25 30

cag gct cca ccc tat acc gat gct cca cct gcc tac tca gag ctc tat 207 Gln Ala Pro Pro Tyr Thr Asp Ala Pro Pro Ala Tyr Ser Glu Leu Tyr 35 40 45

cgt ccg agc ttt gtg cac cca ggg gct gcc aca gtc ccc acc atg tca 255 Arg Pro Ser Phe Val His Pro Gly Ala Ala Thr Val Pro Thr Met Ser 50 55 60

gcc gca ttt cct gga gcc tct ctg tat ctt ccc atg gcc cag tct gtg 303 Ala Ala Phe Pro Gly Ala Ser Leu Tyr Leu Pro Met Ala Gln Ser Val 65 70 75

gct gtt ggg cct tta ggt tcc aca atc ccc atg gct tat tat cca gtc 351 Ala Val Gly Pro Leu Gly Ser Thr lle Pro Met Ala Tyr Tyr Pro Val 80 85 90

ggt ccc atc tat cca cct ggc tcc aca gtg ctg gtg gaa gga ggg tat 399

| Gly Pro lle Tyr Pro 6 Gly Ser Thr Val Leu Val Glu Gly Tyr 95 100 105  |  |
|---|--|
| gat gca ggt gcc aga ttt gga gct ggg gct act gct ggc aac att cct 447<br>Asp Ala Gly Ala Arg Phe Gly Ala Gly Ala Thr Ala Gly Asn Ile Pro<br>115 120 125 |  |
| cct cca cct cct gga tgc cct ccc aat gct gct cag ctt gca gtc atg Pro Pro Pro Pro Gly Cys Pro Pro Asn Ala Ala Gln Leu Ala Val Met 130 135 140           |  |
| cag gga gcc aac gtc ctc gta act cag cgg aag ggg aac ttc ttc atg 543<br>Gln Gly Ala Asn Val Leu Val Thr Gln Arg Lys Gly Asn Phe Phe Met<br>145 150 155 |  |
| ggt ggt tca gat ggt ggc tac acc atc tgg tgaggaacca aggccacctc 593<br>Gly Gly Ser Asp Gly Gly Tyr Thr lle Trp<br>160 165                               |  |
| tgtgccggga aagacatcac ataccttcag cacttctcac aatgtaactg ctttagtcat 653   |  |
| attaacctga agttgcagtt tagacacatg ttgttggggt gtctttctgg tgcccaaact 713   |  |
| ttcaggcact tttcaaattt aataaggaac catgtaatgg tagcagtacc tccctaaagc 773   |  |
| attttgaggt aggggaggta tccattcata aaatgaatgt gggtgaagcc gccctaagga 833   |  |
| ttttccttta atttctctgg agtaatactg taccatactg gtctttgctt ttagtaataa 893   |  |
| aacatcaaat taggtttgga gggaactttg atcttcctaa gaattaaagt tgccaaatta 953   |  |
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| tagtcttcca tttcctcccg ccagtctcca ttgaatcaat ggtgcaggac agaaagccag 1133  |  |
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Tyr Glu lle Arg Gln Tyr Val Val Gln Val lle Phe Ser Val Thr Phe 35 40 45

Ala Phe Ser Cys Thr Met Phe Glu Leu IIe IIe Phe Glu IIe Leu Gly 50 55 60

Val Leu Asn Ser Ser Ser Arg Tyr Phe His Trp Lys Met Asn Leu Cys 65 70 75 80

Val lle Leu Leu lle Leu Val Phe Met Val Pro Phe Tyr lle Gly Tyr 85 90 95

Phe lie Val Ser Asn lie Arg Leu Leu His Lys Gln Arg Leu Leu Phe 100 - 105 110

Ser Cys Leu Leu Trp Leu Thr Phe Met Tyr Phe Phe Trp Lys Leu Gly 115 120 125

Asp Pro Phe Pro IIe Leu Ser Pro Lys His Gly IIe Leu Ser IIe Glu 130 135 140

Gln Leu lle Ser Arg Val Gly Val lle Gly Val Thr Leu Met Ala Leu 145 150 155 160

Leu Ser Gly Phe Gly Ala Val Asn Cys Pro Tyr Thr Tyr Met Ser Tyr 165 170 175

Phe Leu Arg Asn Val Thr Asp Thr Asp Ile Leu Ala Leu Glu Arg Arg 180 185 190

Leu Leu Gln Thr Met Asp Met lle lle Ser Lys Lys Arg Met Ala 195 200 205

Met Ala Arg Arg Thr Met Phe Gln Lys Gly Glu Val His Asn Lys Pro 210 215 220

Ser Gly Phe Trp Gly Met lle Lys Ser Val Thr Thr Ser Ala Ser Gly 225 230 235 240

Ser Glu Asn Leu Thr Leu lle Gln Gln Glu Val Asp Ala Leu Glu Glu



Leu Ser Arg Gin Leu Phe Leu Glu Thr Ala Asp Leu Tyr Ala Thr Lys 260 265 270

Glu Arg Ile Glu Tyr Ser Lys Thr Phe Lys Gly Lys Tyr Phe Asn Phe 275 280 285

Leu Gly Tyr Phe Phe Ser lle Tyr Cys Val Trp Lys lle Phe Met Ala 290 295 300

Thr lie Asn lie Val Phe Asp Arg Val Gly Lys Thr Asp Pro Val Thr 305 310 315 320

Arg Gly lle Glu lle Thr Val Asn Tyr Leu Gly lle Gln Phe Asp Val 325 330 335

Lys Phe Trp Ser Gln His Ile Ser Phe Ile Leu Val Gly Ile Ile Ile 340 345 350

Val Thr Ser lle Arg Gly Leu Leu lle Thr Leu Thr Lys Phe Phe Tyr 355 360 365

Ala lle Ser Ser Ser Lys Ser Ser Asn Val lle Val Leu Leu Leu Ala 370 380

Gln lle Met Gly Met Tyr Phe Val Ser Ser Val Leu Leu lle Arg Met 385 390 395 400

Ser Met Pro Leu Glu Tyr Arg Thr lle lle Thr Glu Val Leu Gly Glu 405 410 415

Leu Gln Phe Asn Phe Tyr His Arg Trp Phe Asp Val IIe Phe Leu Val 420 425 430

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|            |           |            |            | gac<br>Asp        |            |            |           |            |                   |            |            |            |            |                   |            | 166 |
|------------|-----------|------------|------------|-------------------|------------|------------|-----------|------------|-------------------|------------|------------|------------|------------|-------------------|------------|-----|
|            |           |            |            | tgg<br>Trp        |            |            |           |            |                   |            |            |            |            |                   |            | 214 |
|            |           |            |            | tat<br>Tyr        |            |            |           |            |                   |            |            |            |            |                   |            | 262 |
|            |           |            |            | atg<br>Met        |            |            |           |            |                   |            |            |            |            |                   |            | 310 |
|            |           |            |            | tcc<br>Ser<br>70  |            |            |           |            |                   |            |            |            |            |                   |            | 358 |
|            |           |            |            | ctg<br>Leu        |            |            |           |            |                   |            |            |            |            |                   |            | 406 |
|            |           |            |            | atc<br>lle        |            |            |           |            |                   |            |            |            |            |                   |            | 454 |
|            |           |            |            | ctg<br>Leu        |            |            |           |            |                   |            |            |            |            |                   |            | 502 |
|            |           |            |            | ctc<br>Leu        |            |            |           |            |                   |            |            |            |            |                   |            | 550 |
| ctc<br>Leu | atc<br>He | agc<br>Ser | cgg<br>Arg | gtt<br>Val<br>150 | ggt<br>Gly | gtg<br>Val | att<br>He | gga<br>Gly | gtg<br>Val<br>155 | act<br>Thr | ctc<br>Leu | atg<br>Met | gct<br>Ala | ctt<br>Leu<br>160 | ctt<br>Leu | 598 |
|            |           |            |            | gct<br>Ala        |            |            |           |            |                   |            |            |            |            |                   |            | 646 |
|            |           |            |            | act<br>Thr        |            |            |           |            |                   |            |            |            |            |                   |            | 694 |
|            |           |            |            | gat<br>Asp        |            |            |           |            |                   |            |            |            |            |                   |            | 742 |
|            |           |            |            | atg<br>Met        |            |            |           |            |                   |            |            |            |            |                   |            | 790 |
|            |           |            |            | atg<br>Met        |            |            |           |            |                   |            |            |            |            |                   |            | 838 |

| gaa<br>Glu        | a aat<br>u Asr        | cti<br>Lei        | t act<br>a Thr<br>245 | · Leu             | att<br>Ille       | caa<br>Glr        | ı cag<br>ı Gln    | gaa<br>Glu<br>250 | Val               | g gat<br>Asp      | gct<br>Ala        | ttg<br>Leu        | gaa<br>Glu<br>255 | Glu               | tta<br>Leu        | 886  |
|-------------------|-----------------------|-------------------|-----------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| ago<br>Ser        | agg<br>Arg            | cag<br>Glr<br>260 | າ Leu                 | : ttt<br>ı Phe    | ctg<br>Leu        | gaa<br>Glu        | aca<br>Thr<br>265 | Ala               | gat<br>Asp        | cta<br>Leu        | tat<br>Tyr        | gct<br>Ala<br>270 | Thr               | aag<br>Lys        | gag<br>Glu        | 934  |
| aga<br>Arg        | a ata<br>g lle<br>275 | : Glu             | a tac<br>ı Tyr        | tcc<br>Ser        | aaa<br>Lys        | acc<br>Thr<br>280 | Phe               | aag<br>Lys        | ggg<br>Gly        | aaa<br>Lys        | tat<br>Tyr<br>285 | ttt<br>Phe        | aat<br>Asn        | ttt<br>Phe        | ctt<br>Leu        | 982  |
| ggt<br>Gly<br>290 | ' lyr                 | ttt<br>Phe        | ttc<br>Phe            | tct<br>Ser        | att<br>Ile<br>295 | Tyr               | tgt<br>Cys        | gtt<br>Val        | tgg<br>Trp        | aaa<br>Lys<br>300 | He                | ttc<br>Phe        | atg<br>Met        | gct<br>Ala        | acc<br>Thr<br>305 | 1030 |
| ato               | aat<br>Asn            | att<br>He         | gtt<br>Val            | ttt<br>Phe<br>310 | Asp               | cga<br>Arg        | gtt<br>Val        | ggg<br>Gly        | aaa<br>Lys<br>315 | acg<br>Thr        | gat<br>Asp        | cct<br>Pro        | gtc<br>Val        | aca<br>Thr<br>320 | aga<br>Arg        | 1078 |
| ggc<br>Gly        | att<br>lle            | gag<br>Glu        | atc<br>lle<br>325     | act<br>Thr        | gtg<br>Val        | aat<br>Asn        | tat<br>Tyr        | ctg<br>Leu<br>330 | gga<br>Gly        | atc<br>Ile        | caa<br>Gln        | ttt<br>Phe        | gat<br>Asp<br>335 | gtg<br>Val        | aag<br>Lys        | 1126 |
| ttt<br>Phe        | tgg<br>Trp            | tcc<br>Ser<br>340 | Gln                   | cac<br>His        | att<br>lle        | tcc<br>Ser        | ttc<br>Phe<br>345 | att<br>lle        | ctt<br>Leu        | gtt<br>Val        | gga<br>Gly        | ata<br>  e<br>350 | atc<br>lle        | atc<br>He         | gtc<br>Val        | 1174 |
| aca<br>Thr        | tcc<br>Ser<br>355     | atc<br>lie        | aga<br>Arg            | gga<br>Gly        | ttg<br>Leu        | ctg<br>Leu<br>360 | atc<br>lle        | act<br>Thr        | ctt<br>Leu        | acc<br>Thr        | aag<br>Lys<br>365 | ttc<br>Phe        | ttt<br>Phe        | tat<br>Tyr        | gcc<br>Ala        | 1222 |
| atc<br>lle<br>370 | tct<br>Ser            | agc<br>Ser        | agt<br>Ser            | aag<br>Lys        | tcc<br>Ser<br>375 | tcc<br>Ser        | aat<br>Asn        | gtc<br>Val        | att<br>He         | gtc<br>Val<br>380 | ctg<br>Leu        | cta<br>Leu        | tta<br>Leu        | gca<br>Ala        | cag<br>Gln<br>385 | 1270 |
| ata<br>Ile        | atg<br>Met            | ggc<br>Gly        | atg<br>Met            | tac<br>Tyr<br>390 | ttt<br>Phe        | gtc<br>Val        | tcc<br>Ser        | tct<br>Ser        | gtg<br>Val<br>395 | ctg<br>Leu        | ctg<br>Leu        | atc<br>lle        | cga<br>Arg        | atg<br>Met<br>400 | agt<br>Ser        | 1318 |
| atg<br>Met        | cct<br>Pro            | tta<br>Leu        | gaa<br>Glu<br>405     | tac<br>Tyr        | cgc<br>Arg        | acc<br>Thr        | ata<br>  e        | atc<br>lle<br>410 | act<br>Thr        | gaa<br>Glu        | gtc<br>Val        | ctt<br>Leu        | gga<br>Gly<br>415 | gaa<br>Glu        | ctg<br>Leu        | 1366 |
| cag<br>Gln        | Phe                   | aac<br>Asn<br>420 | ttc<br>Phe            | tat<br>Tyr        | cac<br>His        | cgt<br>Arg        | tgg<br>Trp<br>425 | ttt<br>Phe        | gat<br>Asp        | gtg<br>Val        | Пe                | ttc<br>Phe<br>430 | ctg<br>Leu        | gtc<br>Val        | agc<br>Ser        | 1414 |
| Ala               | ctc<br>Leu<br>435     | tct<br>Ser        | agc<br>Ser            | ata<br>He         | Leu               | ttc<br>Phe<br>440 | ctc<br>Leu        | tat<br>Tyr        | ttg<br>Leu        | Ala               | cac<br>His<br>445 | aaa<br>Lys        | cag<br>G n        | gca<br>Ala        | cca<br>Pro        | 1462 |
| gag<br>Glu<br>450 | aag<br>Lys            | caa<br>G n        | atg<br>Met            | Ala               | cct<br>Pro<br>455 | tgaa              | ctta              | ag c              | ctac              | taca              | g ac              | tgtt              | agag              |                   |                   | 1510 |

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Gly Ala Ala Asp Lys Ser Ala Val Val Ala Ala Ala Ala Pro Ala Ser 35 40 45

Val Ala Asp Asp Thr Pro Pro Pro Glu Arg Arg Asn Lys Ser Gly 11e 50 55 60

lle Ser Glu Pro Leu Asn Lys Ser Leu Arg Arg Ser Arg Pro Leu Ser 65 70 75 80

His Tyr Ser Ser Phe Gly Ser Ser Gly Gly Ser Gly Gly Ser Met 85 90 95

Met Gly Gly Glu Ser Ala Asp Lys Ala Thr Ala Ala Ala Ala Ala Ala 100 105 110

Ser Leu Leu Ala Asn Gly His Asp Leu Ala Ala Met Ala Val Asp 115 120 125

Lys Ser Asn Pro Thr Ser Lys His Lys Ser Gly Ala Val Ala Ser Leu 130 135 140

Leu Ser Lys Ala Glu Arg Ala Thr Glu Leu Ala Ala Glu Gly Gln Leu 145 150 155 160

Thr Leu Gin Gin Phe Ala Gin Ser Thr Glu Met Leu Lys Arg Val 165 170 175

Gin Glu His Leu Pro Leu Met Ser Glu Ala Gly Ala Gly Leu Pro Asp 180 185 190

Met Glu Ala Val Ala Gly Ala Glu Ala Leu Asn Gly Gln Ser Asp Phe



Pro Tyr Leu Gly Ala Phe Pro 11e Asn Pro Gly Leu Phe 11e Met Thr 210

Pro Ala Gly Val Phe Leu Ala Glu Ser Ala Leu His Met Ala Gly Leu 230

Ala Glu Tyr Pro Met Gln Gly Glu Leu Ala Ser Ala IIe Ser Ser Gly 255

Lys Lys Lys Arg Lys Arg Cys Gly Met Cys Ala Pro Cys Arg Arg 270

Ile Asn Cys Glu Gln Cys Ser Ser Cys Arg Asn Arg Lys Thr Gly His 290

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agc ctc ggc ggt ggc tcc cag gat gcc ggc ggc agt agc agc agc agc 345 Ser Leu Gly Gly Ser Gln Asp Ala Gly Gly Ser Ser Ser Ser 5

acc aat ggc agc ggt ggc agt ggc agc agt ggc cca aag gca gga gca
Thr Asn Gly Ser Gly Gly Ser Gly Ser Ser Gly Pro Lys Ala Gly Ala
20 25 30

gca gac aag agt gca gtg gtg gct gcc gca cca gcc tca gtg gca 441

| Ala<br>35         | Asp               | Lys               | Ser               | Ala               | 40                  | Val               | Ala               | Ala               | Ala               | Ala<br>45         | Pro               | Ala               |                   | Val               | Ala<br>50         |      |
|-------------------|-------------------|-------------------|-------------------|-------------------|---------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| gat<br>Asp        | gac<br>Asp        | aca<br>Thr        | cca<br>Pro        | ccc<br>Pro<br>55  | ccc<br>Pro          | gag<br>Glu        | cgt<br>Arg        | cgg<br>Arg        | aac<br>Asn<br>60  | aag<br>Lys        | agc<br>Ser        | ggt<br>Gly        | atc<br>Ile        | atc<br>Ile<br>65  | agt<br>Ser        | 489  |
| gag<br>Glu        | ccc<br>Pro        | ctc<br>Leu        | aac<br>Asn<br>70  | aag<br>Lys        | agc<br>Ser          | ctg<br>Leu        | cgc<br>Arg        | cgc<br>Arg<br>75  | tcc<br>Ser        | cgc<br>Arg        | ccg<br>Pro        | ctc<br>Leu        | tcc<br>Ser<br>80  | cac<br>His        | tac<br>Tyr        | 537  |
| tct<br>Ser        | tct<br>Ser        | ttt<br>Phe<br>85  | ggc<br>Gly        | agc<br>Ser        | agt<br>Ser          | ggt<br>Gly        | ggt<br>Gly<br>90  | agt<br>Ser        | ggc<br>Gly        | ggt<br>Gly        | ggc<br>Gly        | agc<br>Ser<br>95  | atg<br>Met        | atg<br>Met        | ggc<br>Gly        | 585  |
| gga<br>Gly        | gag<br>Glu<br>100 | tct<br>Ser        | gct<br>Ala        | gac<br>Asp        | a <b>a</b> g<br>Lys | gcc<br>Ala<br>105 | act<br>Thr        | gcg<br>Ala        | gct<br>Ala        | gca<br>Ala        | gcc<br>Ala<br>110 | gct<br>Ala        | gcc<br>Ala        | tcc<br>Ser        | ctg<br>Leu        | 633  |
| ttg<br>Leu<br>115 | gcc<br>Ala        | aat<br>Asn        | ggg<br>Gly        | cat<br>His        | gac<br>Asp<br>120   | ctg<br>Leu        | gcg<br>Ala        | gcg<br>Ala        | gcc<br>Ala        | atg<br>Met<br>125 | gcg<br>Ala        | gtg<br>Val        | gac<br>Asp        | aaa<br>Lys        | agc<br>Ser<br>130 | 681  |
| aac<br>Asn        | cct<br>Pro        | acc<br>Thr        | tca<br>Ser        | aag<br>Lys<br>135 | cac<br>His          | aaa<br>Lys        | agt<br>Ser        | ggt<br>Gly        | gct<br>Ala<br>140 | gtg<br>Val        | gcc<br>Ala        | agc<br>Ser        | ctg<br>Leu        | ctg<br>Leu<br>145 | agc<br>Ser        | 729  |
| aag<br>Lys        | gca<br>Ala        | gag<br>Glu        | cgg<br>Arg<br>150 | gcc<br>Ala        | acg<br>Thr          | gag<br>Glu        | ctg<br>Leu        | gca<br>Ala<br>155 | gcc<br>Ala        | gag<br>Glu        | gga<br>Gly        | cag<br>Gln        | ctg<br>Leu<br>160 | acg<br>Thr        | ctg<br>Leu        | 777  |
|                   |                   |                   |                   |                   |                     | aca<br>Thr        |                   |                   |                   |                   |                   |                   |                   |                   |                   | 825  |
| cat<br>His        | ctc<br>Leu<br>180 | ccg<br>Pro        | ctg<br>Leu        | atg<br>Met        | agc<br>Ser          | gag<br>Glu<br>185 | gcg<br>Ala        | ggt<br>Gly        | gct<br>Ala        | ggc<br>Gly        | ctg<br>Leu<br>190 | cct<br>Pro        | gac<br>Asp        | atg<br>Met        | gag<br>Glu        | 873  |
| gct<br>Ala<br>195 | gtg<br>Val        | gca<br>Ala        | ggt<br>Gly        | gcc<br>Ala        | gaa<br>Glu<br>200   | gcc<br>Ala        | ctc<br>Leu        | aat<br>Asn        | ggc<br>Gly        | cag<br>Gln<br>205 | tcc<br>Ser        | gac<br>Asp        | ttc<br>Phe        | ccc<br>Pro        | tac<br>Tyr<br>210 | 921  |
| ctg<br>Leu        | ggc<br>Gly        | gct<br>Ala        | ttc<br>Phe        | ccc<br>Pro<br>215 | atc<br>Ile          | aac<br>Asn        | cca<br>Pro        | ggc<br>Gly        | ctc<br>Leu<br>220 | ttc<br>Phe        | att<br>lle        | atg<br>Met        | acc<br>Thr        | ccg<br>Pro<br>225 | gca<br>Ala        | 969  |
| ggt<br>Gly        | gtg<br>Val        | ttc<br>Phe        | ctg<br>Leu<br>230 | gcc<br>Ala        | gag<br>Glu          | agc<br>Ser        | gcg<br>Ala        | ctg<br>Leu<br>235 | cac<br>His        | atg<br>Met        | gcg<br>Ala        | ggc<br>Gly        | ctg<br>Leu<br>240 | gct<br>Ala        | gag<br>Glu        | 1017 |
| tac<br>Tyr        | ccc<br>Pro        | atg<br>Met<br>245 | cag<br>Gln        | gga<br>Gly        | gag<br>Glu          | ctg<br>Leu        | gcc<br>Ala<br>250 | tct<br>Ser        | gcc<br>Ala        | atc<br>Ile        | agc<br>Ser        | tcc<br>Ser<br>255 | ggc<br>Gly        | aag<br>Lys        | aag<br>Lys        | 1065 |
| aag<br>Lys        | cgg<br>Arg<br>260 | aaa<br>Lys        | cgc<br>Arg        | tgc<br>Cys        | ggc<br>Gly          | atg<br>Met<br>265 | tgc<br>Cys        | gcg<br>Ala        | ccc<br>Pro        | tgc<br>Cys        | cgg<br>Arg<br>270 | cgg<br>Arg        | cgc<br>Arg        | atc<br>Ile        | aac<br>Asn        | 1113 |

|   |            |            | - (       |            |            |            |            |           |            |            |            |            |                  |            |      |
|---|------------|------------|-----------|------------|------------|------------|------------|-----------|------------|------------|------------|------------|------------------|------------|------|
| tgc gag<br>Cys Glu<br>275   |            |            |           |            |            |            |            |           |            |            |            |            |                  |            | 1161 |
| tgc aaa<br>Cys Lys  |            |            |           |            |            |            |            |           |            |            |            |            |                  |            | 1209 |
| ctg gag<br>Leu Glu  |            |            |           |            |            |            |            |           |            |            |            |            |                  |            | 1257 |
| tgacggc   | ggc        | ggaa       | ccca      | aa go      | ctgc       | ctct       | t cc       | gtgca     | aatg       | tcad       | etgct      | tcg 1      | tgtgg            | gtctcc     | 1317 |
| agcaagggat tcgggcgaag acaaacggat gcacccgtct ttagaaccaa aaatattctc 1 |            |            |           |            |            |            |            |           |            |            |            |            |                  |            | 1377 |
| tcacagattt cattcctgtt tttatatata tatttttgt tgtcgtttta acatctccac 1  |            |            |           |            |            |            |            |           |            |            |            |            |                  |            | 1437 |
|   |            |            |           |            |            |            |            |           |            |            |            |            |                  | 1448       |      |
| <210> 3<br><211> 3<br><212> P<br><213> H                            | 13<br>RT   | sapie      | ens       |            |            |            |            |           |            |            |            |            |                  |            |      |
| <400> 3<br>Met Ala<br>1   |            | Gln        | Pro<br>5  | Gly        | His        | Met        | Pro        | His<br>10 | Gly        | Gly        | Ser        | Ser        | <b>Asn</b><br>15 | Asn        |      |
| Leu Cys   | His        | Thr<br>20  | Ļeu       | Gly        | Pro        | Val        | His<br>25  | Pro       | Pro        | Asp        | Pro        | Gln<br>30  | Arg              | His        |      |
| Pro Asn   | Thr<br>35  | Leu        | Ser       | Phe        | Arg        | Cys<br>40  | Ser        | Leu       | Ala        | Asp        | Phe<br>45  | Gln        | lle              | Glu        |      |
| Lys Lys<br>50   | lle        | Gly        | Arg       | Gly        | G n<br>55  | Phe        | Ser        | Glu       | Val        | Tyr<br>60  | Lys        | Ala        | Thr              | Cys        |      |
| Leu Leu<br>65   | Asp        | Arg        | Lys       | Thr<br>70  | Val        | Ala        | Leu        | Lys       | Lys<br>75  | Val        | Gln        | lle        | Phe              | Glu<br>80  |      |
| Met Met   | Asp        | Ala        | Lys<br>85 | Ala        | Arg        | Gln        | Asp        | Cys<br>90 | Val        | Lys        | Glu        | lle        | Gly<br>95        | Leu        |      |
| Leu Lys   | Gln        | Leu<br>100 | Asn       | His        | Pro        | Asn        | lle<br>105 | lle       | Lys        | Tyr        | Leu        | Asp<br>110 | Ser              | Phe        |      |
| lle Glu   | Asp<br>115 | Asn        | Glu       | Leu        | Asn        | 11e<br>120 | Val        | Leu       | Glu        | Leu        | Ala<br>125 | Asp        | Ala              | Gly        |      |
| Asp Leu<br>130  | Ser        | Gln        | Met       | He         | Lys<br>135 | Tyr        | Phe        | Lys       | Lys        | GIn<br>140 | Lys        | Arg        | Leu              | lle        |      |
| Pro Glu<br>145  | Arg        | Thr        | Val       | Trp<br>150 | Lys        | Tyr        | Phe        | Val       | G n<br>155 | Leu        | Cys        | Ser        | Ala              | Val<br>160 |      |
|   |            |            |           |            |            |            |            |           |            |            |            |            |                  |            |      |

| GΙ        | u H   | is              | Met              | His        | Se<br>165  | g          | Arg              | Val              | Met         | His<br>170 | Arg        | Asp              | Пе               |            | Pro<br>175 | Ala        |     |
|-----------|---|-----------------|------------------|------------|------------|------------|------------------|------------------|-------------|------------|------------|------------------|------------------|------------|------------|------------|-----|
| As        | n V   | al              | Phe              | lle<br>180 | Thr        | Ala        | Thr              | Gly              | Va l<br>185 | Val        | Lys        | Leu              | Gly              | Asp<br>190 | Leu        | Gly        |     |
| Le        | u G   | lу              | Arg<br>195       | Phe        | Phe        | Ser        | Ser              | Glu<br>200       | Thr         | Thr        | Ala        | Ala              | His<br>205       | Ser        | Leu        | Val        |     |
| G۱        |   | hr<br>10        | Pro              | Tyr        | Tyr        | Met        | Ser<br>215       | Pro              | Glu         | Arg        | lle        | His<br>220       | Glu              | Asn        | Gly        | Tyr        |     |
| As<br>22  |   | he              | Lys              | Ser        | Asp        | lle<br>230 | Trp              | Ser              | Leu         | Gly        | Cys<br>235 | Leu              | Leu              | Tyr        | Glu        | Met<br>240 |     |
| ΑI        | a A   | la              | Leu              | Gln        | Ser<br>245 | Pro        | Phe              | Tyr              | Gly         | Asp<br>250 | Lys        | Met              | Asn              | Leu        | Phe<br>255 | Ser        |     |
| Lε        | eu C  | ys              | Gln              | Lys<br>260 | He         | Glu        | Gln              | Cys              | Asp<br>265  | Tyr        | Pro        | Pro              | Leu              | Pro<br>270 | Gly        | Glu        |     |
| Hi        | s T   | yr              | Ser<br>275       | Glu        | Lys        | Leu        | Arg              | Glu<br>280       | Leu         | Val        | Ser        | Met              | Cys<br>285       | lle        | Cys        | Pro        |     |
| As        |   | Pro<br>290      | His              | Gln        | Arg        | Pro        | Asp<br>295       | lle              | Gly         | Tyr        | Val        | His<br>300       | Gln              | Val        | Ala        | Lys        |     |
| G 1<br>30 |   | let             | His              | lle        | Trp        | Met<br>310 | Ser              | Ser              | Thr         |            |            |                  |                  |            |            |            |     |
| <2<br><2  | <210> 40<br><211> 1597<br><212> DNA<br><213> Homo sapiens |                 |                  |            |            |            |                  |                  |             |            |            |                  |                  |            |            |            |     |
| <2        | 220><br>221><br>222>                                      | CE              |                  | . (10      | 091)       |            |                  |                  |             |            |            |                  |                  |            |            |            |     |
|           | 100><br>gcgg  |                 |                  | agct;      | gacgį      | gg cį      | gtgc             | ggċc             | g ct        | gcgc       | cgca       | aac              | tcgt             | gtg        | ggac       | gcaccg     | 60  |
| ct        | cca   | agco            | cgc (            | ccgc       | gggc       | ca go      | cgca             | ccgg             | t cc        | ccca       | gcgg       | cag              | ccga             | gcc (      | cgcc       | cgcgcg     | 120 |
| cc        | gtt   | cgt             | tgc (            | cctc       | gtga       | gg c       | tggc.            | atgc.            | a gg        |            |            |                  |                  |            | ggc<br>Gly |            | 173 |
| at<br>Me  | g c<br>et F   | ccc<br>Pro      | cat<br>His<br>10 | gga<br>Gly | ggg<br>Gly | agt<br>Ser | tcc<br>Ser       | aac<br>Asn<br>15 | aac<br>Asn  | ctc<br>Leu | tgc<br>Cys | cac<br>His       | acc<br>Thr<br>20 | ctg<br>Leu | ggg<br>Gly | cct<br>Pro | 221 |
| g t<br>Vá | g c   | at<br>lis<br>25 | cct<br>Pro       | cct<br>Pro | gac<br>Asp | cca<br>Pro | cag<br>Gln<br>30 | agg<br>Arg       | cat<br>His  | ccc<br>Pro | aac<br>Asn | acg<br>Thr<br>35 | ctg<br>Leu       | tct<br>Ser | ttt<br>Phe | cgc<br>Arg | 269 |
| ts        | rc t  | Cg              | ctg              | āCā        | gac        | ttc        | cag              | atc              | gaa         | aag        | aag        | ata              | ggc              | cga        | gga        | cag        | 317 |

| Cys<br>40         | Ser               | Leu               | ı Ala             | Asp               |                   | Glr               | ılle              | e Glu             | ı Lys             | Lys<br>50         |                   | e Gly             | / A               | ly                   | Gln<br>55         |     |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|----------------------|-------------------|-----|
| ttc<br>Phe        | ago<br>Ser        | gag<br>Glu        | g gtg<br>ı Val    | tac<br>Tyr<br>60  | Lys               | gcc               | acc<br>Thr        | tgo<br>Cys        | ctg<br>Leu<br>65  | ı Let             | g gad<br>ı Asp    | agg<br>Arg        | g aag<br>g Lys    | g aca<br>s Thr<br>70 |                   | 365 |
| gct<br>Ala        | ctg<br>Leu        | aag<br>Lys        | aag<br>Lys<br>75  | Val               | cag<br>Gin        | ato               | ttt<br>Phe        | gag<br>Glu<br>80  | ı Met             | g atg<br>Met      | g gac<br>: Asp    | gcc<br>Ala        | aag<br>Lys<br>85  | Ala                  | agg<br>Arg        | 413 |
| cag<br>Gln        | gac<br>Asp        | tgt<br>Cys<br>90  | Val               | aag<br>Lys        | gag<br>Glu        | atc               | ggo<br>Gly<br>95  | Leu               | ttg<br>Leu        | ; aag<br>Lys      | caa<br>Gln        | ctg<br>Leu<br>100 | Asr               | cac<br>His           | cca<br>Pro        | 461 |
| aat<br>Asn        | atc<br>  e<br>105 | He                | aag<br>Lys        | tat<br>Tyr        | ttg<br>Leu        | gac<br>Asp<br>110 | Ser               | ttt<br>Phe        | atc<br>lle        | gaa<br>Glu        | gac<br>Asp<br>115 | Asn               | gag<br>Glu        | ctg<br>Leu           | aac<br>Asn        | 509 |
| att<br>He<br>120  | Val               | ctg<br>Leu        | gag<br>Glu        | ttg<br>Leu        | gct<br>Ala<br>125 | gac<br>Asp        | gca<br>Ala        | ggg<br>Gly        | gac<br>Asp        | ctc<br>Leu<br>130 | Ser               | cag<br>Gln        | atg<br>Met        | atc<br>lle           | aag<br>Lys<br>135 | 557 |
| tac<br>Tyr        | ttt<br>Phe        | aag<br>Lys        | aag<br>Lys        | cag<br>Gln<br>140 | Lys               | cgg<br>Arg        | ctc<br>Leu        | atc<br>lle        | ccg<br>Pro<br>145 | gag<br>G u        | agg<br>Arg        | aca<br>Thr        | gta<br>Val        | tgg<br>Trp<br>150    | aag<br>Lys        | 605 |
| tac<br>Tyr        | ttt<br>Phe        | gtg<br>Val        | cag<br>Gin<br>155 | ctg<br>Leu        | tgc<br>Cys        | agc<br>Ser        | gcc<br>Ala        | gtg<br>Val<br>160 | gag<br>Glu        | cac<br>His        | atg<br>Met        | cat<br>His        | tca<br>Ser<br>165 | cgc<br>Arg           | cgg<br>Arg        | 653 |
| gtg<br>Val        | atg<br>Met        | cac<br>His<br>170 | cga<br>Arg        | _gac<br>Asp       | atc<br>lle        | aag<br>Lys        | cct<br>Pro<br>175 | gcc<br>Ala        | aac<br>Asn        | gtg<br>Val        | ttc<br>Phe        | atc<br>  e<br>180 | aca<br>Thr        | gcc<br>Ala           | acg<br>Thr        | 701 |
| ggc<br>Gly        | gtc<br>Val<br>185 | gtg<br>Val        | aag<br>Lys        | ctc<br>Leu        | ggt<br>Gly        | gac<br>Asp<br>190 | ctt<br>Leu        | ggt<br>Gly        | ctg<br>Leu        | ggc<br>Gly        | cgc<br>Arg<br>195 | ttc<br>Phe        | ttc<br>Phe        | agc<br>Ser           | tct<br>Ser        | 749 |
| gag<br>Glu<br>200 | acc<br>Thr        | acc<br>Thr        | gca<br>Ala        | gcc<br>Ala        | cac<br>His<br>205 | tcc<br>Ser        | cta<br>Leu        | gtg<br>Val        | ggg<br>Gly        | acg<br>Thr<br>210 | ccc<br>Pro        | tac<br>Tyr        | tac<br>Tyr        | atg<br>Met           | tca<br>Ser<br>215 | 797 |
| ccg<br>Pro        | gag<br>Glu        | agg<br>Arg        | atc<br>lle        | cat<br>His<br>220 | gag<br>Glu        | aac<br>Asn        | ggc<br>Gly        | tac<br>Tyr        | aac<br>Asn<br>225 | ttc<br>Phe        | aag<br>Lys        | tcc<br>Ser        | gac<br>Asp        | atc<br>  e<br>230    | tgg<br>Trp        | 845 |
| tcc<br>Ser        | ttg<br>Leu        | ggc<br>Gly        | tgt<br>Cys<br>235 | ctg<br>Leu        | ctg<br>Leu        | tac<br>Tyr        | gag<br>Glu        | atg<br>Met<br>240 | gca<br>Ala        | gcc<br>Ala        | ctc<br>Leu        | cag<br>Gln        | agc<br>Ser<br>245 | ccc<br>Pro           | ttc<br>Phe        | 893 |
| at                | gga<br>Gly        | gat<br>Asp<br>250 | aag<br>Lys        | atg<br>Met        | aat<br>Asn        | ctc<br>Leu        | ttc<br>Phe<br>255 | tcc<br>Ser        | ctg<br>Leu        | tgc<br>Cys        | cag<br>Gln        | aag<br>Lys<br>260 | atc<br>Ile        | gag<br>Glu           | cag<br>Gln        | 941 |
| ys                | gac<br>Asp<br>265 | tac<br>Tyr        | ccc<br>Pro        | cca<br>Pro        | Leu               | ccc<br>Pro<br>270 | ggg<br>Gly        | gag<br>Glu        | cac<br>His        | tac<br>Tyr        | tcc<br>Ser        | gag<br>Glu        | aag<br>Lys        | tta<br>Leu           | cga<br>Arg        | 989 |

|   | gaa ctg gtc agc atg tgc atc tgc cct gac ccc cac cag aga cct gac<br>Glu Leu Val Ser Met Cys IIe Cys Pro Asp Pro His Gln Arg Pro Asp<br>280 285 290 295 | 1037 |
|---|---|------|
| • | atc gga tac gtg cac cag gtg gcc aag cag atg cac atc tgg atg tcc<br>lle Gly Tyr Val His Gln Val Ala Lys Gln Met His lle Trp Met Ser<br>300 305 310     | 1085 |
|   | agc acc tgagcgtgga tgcaccgtgc cttatcaaag ccagcaccac tttgccttac<br>Ser Thr   | 1141 |
|   | ttgagtcgtc ttctcttcga gtggccacct ggtagcctag aacagctaag accacagggt   | 1201 |
|   | tcagcaggtt ccccaaaagg ctgcccagcc ttacagcaga tgctgaaggc agagcagctg   | 1261 |
|   | agggagggc gctggccaca tgtcactgat ggtcagattc caaagtcctt tctttatact  | 1321 |
|   | gttgtggaca atctcagctg ggtcaataag ggcaggtggt tcagcgagcc acggcagccc   | 1381 |
|   | cctgtatctg gattgtaatg tgaatcttta gggtaattcc tccagtgacc tgtcaaggct   | 1441 |
|   | tatgctaaca ggagacttgc aggagaccgt gtgatttgtg tagtgagcct ttgaaaatgg   | 1501 |
|   | ttagtaccgg gttcagttta gttcttggta tcttttcaat caagctgtgt gcttaattta   | 1561 |
|   | ctctgttgta aagggataaa gtggaaatca ttttt  | 1597 |
|   | <210> 41  |      |

<211> 371

<212> PRT

<213> Homo sapiens

<400> 41

Met Ser His Glu Lys Ser Phe Leu Val Ser Gly Asp Asn Tyr Pro Pro 1 5 10 15

Pro Asn Pro Gly Tyr Pro Gly Gly Pro Gln Pro Pro Met Pro Pro Tyr 20 25 30

Ala Gln Pro Pro Tyr Pro Gly Ala Pro Tyr Pro Gln Pro Pro Phe Gln 35 40 45

Pro Ser Pro Tyr Gly Gln Pro Gly Tyr Pro His Gly Pro Ser Pro Tyr 50 55 60

Pro Gln Gly Gly Tyr Pro Gln Gly Pro Tyr Pro Gln Gly Gly Tyr Pro 65 70 75 80

Gln Gly Pro Tyr Pro Gln Glu Gly Tyr Pro Gln Gly Pro Tyr Pro Gln 85 90 95

Gly Gly Tyr Pro Gln Gly Pro Tyr Pro Gln Ser Pro Phe Pro Pro Asn 100 105 110

Pro Tyr Gly Gln Pro Gln Val Phe Pro Gly Gln Asp Pro Asp Ser Pro 115 120 125 Gln His Gly Asn Tyr Gln Glu Glu Gly Pro Pro Ser Tyr Tyr Asp Asn 130 135 140

Gln Asp Phe Pro Ala Thr Asn Trp Asp Asp Lys Ser Ile Arg Gln Ala 145 150 155 160

Phe lle Arg Lys Val Phe Leu Val Leu Thr Leu Gln Leu Ser Val Thr 165 170 175

Leu Ser Thr Val Ser Val Phe Thr Phe Val Ala Glu Val Lys Gly Phe 180 185 190

Val Arg Glu Asn Val Trp Thr Tyr Tyr Val Ser Tyr Ala Val Phe Phe 195 200 205

lle Ser Leu lle Val Leu Ser Cys Cys Gly Asp Phe Arg Arg Lys His 210 215 220

Pro Trp Asn Leu Val Ala Leu Ser Val Leu Thr Ala Ser Leu Ser Tyr 225 230 235 240

Met Val Gly Met IIe Ala Ser Phe Tyr Asn Thr Glu Ala Val IIe Met 245 250 255

Ala Val Gly lle Thr Thr Ala Val Cys Phe Thr Val Val lle Phe Ser 260 265 270

Met Gln Thr Arg Tyr Asp Phe Thr Ser Cys Met Gly Val Leu Leu Val 275 280 285

Ser Met Val Val Leu Phe IIe Phe Ala IIe Leu Cys IIe Phe IIe Arg 290 295 300

Asn Arg IIe Leu Glu IIe Val Tyr Ala Ser Leu Gly Ala Leu Leu Phe 305 310 315 320

Thr Cys Phe Leu Ala Val Asp Thr Gln Leu Leu Leu Gly Asn Lys Gln 325 330 335

Leu Ser Leu Ser Pro Glu Glu Tyr Val Phe Ala Ala Leu Asn Leu Tyr 340 345 350

Thr Asp IIe IIe Asn IIe Phe Leu Tyr IIe Leu Thr IIe IIe Gly Arg 355 360 365

Ala Lys Glu 370

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<211> 1781

<212> DNA

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<222> (91).. (1203)

| <pre>&lt;400&gt; 42 attggccatc accgcgcggc cgcgcagcgg acaccgtgcg taccggcctg cggcgcccgg 6</pre> |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | 60                |                   |     |
|---|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-----|
| сса   | ccgg              | ggc g             | ggac              | egegg             | ga ad             | ccga              | aggco             | atg<br>Met        | g too<br>Ser      | c cat             | t gaa<br>s Glu    | a aag<br>u Lys    | g agt<br>s Sei    | ttt<br>Phe        | t ttg<br>e Leu    | 114 |
| gtg<br>Val  | tct<br>Ser<br>10  | ggg<br>Gly        | gac<br>Asp        | aac<br>Asn        | tat<br>Tyr        | cct<br>Pro<br>15  | ccc<br>Pro        | ccc<br>Pro        | aac<br>Asn        | cct<br>Pro        | gga<br>Gly<br>20  | tat<br>Tyr        | ccg<br>Pro        | ggg<br>Gly        | ggg<br>Gly        | 162 |
| ccc<br>Pro<br>25  | cag<br>Gln        | cca<br>Pro        | ccc<br>Pro        | atg<br>Met        | ccc<br>Pro<br>30  | ccc<br>Pro        | tat<br>Tyr        | gct<br>Ala        | cag<br>Gln        | cct<br>Pro<br>35  | ccc<br>Pro        | tac<br>Tyr        | cct<br>Pro        | ggg<br>Gly        | gcc<br>Ala<br>40  | 210 |
|   | tac<br>Tyr        |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | 258 |
|   | ccc<br>Pro        |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | 306 |
| ccc<br>Pro  | tac<br>Tyr        | ccc<br>Pro<br>75  | caa<br>Gln        | ggg<br>Gly        | ggc<br>Gly        | tac<br>Tyr        | cca<br>Pro<br>80  | cag<br>Gln        | ggc<br>Gly        | ccc<br>Pro        | tac<br>Tyr        | cca<br>Pro<br>85  | caa<br>Gln        | gag<br>Glu        | ggc<br>Gly        | 354 |
|   | cca<br>Pro<br>90  |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | 402 |
|   | cag<br>Gln        |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | 450 |
| cca<br>Pro  | gga<br>Gly        | caa<br>G n        | gac<br>Asp        | cct<br>Pro<br>125 | gac<br>Asp        | tca<br>Ser        | ccc<br>Pro        | cag<br>Gln        | cat<br>His<br>130 | gga<br>Gly        | aac<br>Asn        | tac<br>Tyr        | cag<br>Gln        | gag<br>Glu<br>135 | gag<br>Glu        | 498 |
| ggt<br>Gly  | ccc<br>Pro        | cca<br>Pro        | tcc<br>Ser<br>140 | tac<br>Tyr        | tat<br>Tyr        | gac<br>Asp        | aac<br>Asn        | cag<br>Gln<br>145 | gac<br>Asp        | ttc<br>Phe        | cct<br>Pro        | gcc<br>Ala        | acc<br>Thr<br>150 | aac<br>Asn        | tgg<br>Trp        | 546 |
| gat<br>Asp  | gac<br>Asp        | aag<br>Lys<br>155 | agc<br>Ser        | atc<br>lle        | cga<br>Arg        | cag<br>Gln        | gcc<br>Ala<br>160 | ttc<br>Phe        | atc<br>lle        | cgc<br>Arg        | aag<br>Lys        | gtg<br>Val<br>165 | ttc<br>Phe        | cta<br>Leu        | gtg<br>Val        | 594 |
| ctg<br>Leu  | acc<br>Thr<br>170 | ttg<br>Leu        | cag<br>Gln        | ctg<br>Leu        | tcg<br>Ser        | gtg<br>Val<br>175 | acc<br>Thr        | ctg<br>Leu        | tcc<br>Ser        | acg<br>Thr        | gtg<br>Val<br>180 | tct<br>Ser        | gtg<br>Val        | ttc<br>Phe        | act<br>Thr        | 642 |
| ttt<br>Phe<br>185   | gtt<br>Val        | gcg<br>Ala        | gag<br>Glu        | gtg<br>Val        | aag<br>Lys<br>190 | ggc<br>Gly        | ttt<br>Phe        | gtc<br>Val        | cgg<br>Arg        | gag<br>Glu<br>195 | aat<br>Asn        | gtc<br>Val        | tgg<br>Trp        | acc<br>Thr        | tac<br>Tyr<br>200 | 690 |
| tat<br>Tyr  | gtc<br>Val        | tcc<br>Ser        | tat<br>Tyr        | gct<br>Ala        | gtc<br>Val        | ttc<br>Phe        | ttc<br>Phe        | atc<br>  e        | tct<br>Ser        | ctc<br>Leu        | atc<br>Ile        | gtc<br>Val        | ctc<br>Leu        | agc<br>Ser        | tgt<br>Cys        | 738 |

|                   |                   |                   |                   |                   | _                 |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |      |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| tgt<br>Cys        | ggg<br>Gly        | gac<br>Asp        | ttc<br>Phe<br>220 | Arg               | cga<br>Arg        | aag<br>Lys        | cac<br>His        | ccc<br>Pro<br>225 | Trp               | aac<br>Asn        | ctt<br>Leu        | gtt<br>Val        | gca<br>Ala<br>230 | Leu               | tcg<br>Ser        | 786  |
| gto<br>Val        | ctg<br>Leu        | acc<br>Thr<br>235 | gcc<br>Ala        | agc<br>Ser        | ctg<br>Leu        | tcg<br>Ser        | tac<br>Tyr<br>240 | atg<br>Met        | gtg<br>Val        | ggg<br>Gly        | atg<br>Met        | atc<br>  e<br>245 | gcc<br>Ala        | agc<br>Ser        | ttc<br>Phe        | 834  |
| tac<br>Tyr        | aac<br>Asn<br>250 | acc<br>Thr        | gag<br>Glu        | gca<br>Ala        | gtc<br>Val        | atc<br>Ile<br>255 | atg<br>Met        | gcc<br>Ala        | gtg<br>Val        | ggc<br>Gly        | atc<br>lle<br>260 | acc<br>Thr        | aca<br>Thr        | gcc<br>Ala        | gtc<br>Val        | 882  |
| tgc<br>Cys<br>265 | ttc<br>Phe        | acc<br>Thr        | gtc<br>Val        | gtc<br>Val        | atc<br>Ile<br>270 | ttc<br>Phe        | tcc<br>Ser        | atg<br>Met        | cag<br>G n        | acc<br>Thr<br>275 | cgc<br>Arg        | tac<br>Tyr        | gac<br>Asp        | ttc<br>Phe        | acc<br>Thr<br>280 | 930  |
| tca<br>Ser        | tgc<br>Cys        | atg<br>Met        | ggc<br>Gly        | gtg<br>Val<br>285 | ctc<br>Leu        | ctg<br>Leu        | gtg<br>Val        | agc<br>Ser        | atg<br>Met<br>290 | gtg<br>Val        | gtg<br>Val        | ctc<br>Leu        | ttc<br>Phe        | atc<br>lle<br>295 | ttc<br>Phe        | 978  |
| gcc<br>Ala        | att<br>He         | Leu               | tgc<br>Cys<br>300 | atc<br>Ile        | ttc<br>Phe        | atc<br>Ile        | cgg<br>Arg        | aac<br>Asn<br>305 | cgc<br>Arg        | atc<br>lle        | ctg<br>Leu        | gag<br>Glu        | atc<br>Ile<br>310 | gtg<br>Val        | tac<br>Tyr        | 1026 |
| gcc<br>Ala        | tca<br>Ser        | ctg<br>Leu<br>315 | ggc<br>Gly        | gct<br>Ala        | ctg<br>Leu        | ctc<br>Leu        | ttc<br>Phe<br>320 | acc<br>Thr        | tgc<br>Cys        | ttc<br>Phe        | ctc<br>Leu        | gca<br>Ala<br>325 | gtg<br>Val        | gac<br>Asp        | acc<br>Thr        | 1074 |
| cag<br>G n        | ctg<br>Leu<br>330 | ctg<br>Leu        | ctg<br>Leu        | ggg<br>Gly        | Asn               | aag<br>Lys<br>335 | cag<br>Gln        | ctg<br>Leu        | tcc<br>Ser        | ctg<br>Leu        | agc<br>Ser<br>340 | cca<br>Pro        | gaa<br>Glu        | gag<br>Glu        | tat<br>Tyr        | 1122 |
| gtg<br>Val<br>345 | ttt<br>Phe        | gct<br>Ala        | gcg<br>Ala        | Leu               | aac<br>Asn<br>350 | ctg<br>Leu        | tac<br>Tyr        | aca<br>Thr        | Asp               | atc<br>  e<br>355 | atc<br>lle        | aac<br>Asn        | atc<br>He         | Phe               | ctg<br>Leu<br>360 | 1170 |
| tac<br>Tyr        | atc<br>lle        | ctc<br>Leu        | Inr               | atc<br>  e<br>365 | att<br>lle        | ggc<br>Gly        | cgc<br>Arg        | Ala               | aag<br>Lys<br>370 | gag<br>Glu        | tagc              | cgag              | ct c              | cagc              | tcgct             | 1223 |
| gtgc              | ccgc              | tc a              | ggtg              | gcac              | g gc              | tggc              | ctgg              | acc               | ctgc              | ссс               | tggc              | acgg              | ca g              | tgcc              | agctg             | 1283 |
| tact              | tccc              | ct c              | tctc              | ttgt              | c cc              | cagg              | caca              | gcc               | tagg              | gaa               | aagg              | atgc              | ct c              | tctc              | саасс             | 1343 |
|                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | gcccc             |      |
|                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | ctgtc             |      |
|                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | accag             |      |
| gtcc              | cgggg             | ga ga             | aggga             | attga             | a gcc             | caaga             | eggt              | gagg              | ggtgo             | cac ;             | gtct              | tccct             | to c              | tgtc              | ccagc             | 1583 |
| tccc              | cagoo             | t gg              | gogta             | igago             | acc               | ccto              | ссс               | tcc               | cccc              | cac (             | cccc              | ctgga             | ag t              | gctgo             | cctc              | 1643 |
| tggg              | gacat             | g cg              | gagt              | gggg              | ggto              | ttat              | ссс               | tgtg              | gctga             | agc (             | cctga             | agggo             | ca ga             | agagg             | gatgg             | 1703 |

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<400> 43

Met Ser Asp Glu Arg Glu Val Ala Glu Ala Ala Thr Gly Glu Asp Ala 1 5 10 15

Ser Ser Pro Pro Pro Lys Thr Glu Ala Ala Ser Asp Pro Gln His Pro 20 25 30

Ala Ala Ser Glu Gly Ala Ala Ala Ala Ala Ala Ser Pro Pro Leu Leu 35 40 45

Arg Cys Leu Val Leu Thr Gly Phe Gly Gly Tyr Asp Lys Val Lys Leu 50 60

Gln Ser Arg Pro Ala Ala Pro Pro Ala Pro Gly Pro Gly Gln Leu Thr 65 70 75 80

Leu Arg Leu Arg Ala Cys Gly Leu Asn Phe Ala Asp Leu Met Ala Arg 85 90 95

Gin Gly Leu Tyr Asp Arg Leu Pro Pro Leu Pro Val Thr Pro Gly Met 100 105 110

Glu Gly Ala Gly Val Val Ile Ala Val Gly Glu Gly Val Ser Asp Arg 115 120 125

Lys Ala Gly Asp Arg Val Met Val Leu Asn Arg Ser Gly Met Trp Gln 130 135 140

Glu Glu Val Thr Val Pro Ser Val Gln Thr Phe Leu Ile Pro Glu Ala 145 150 155 160

Met Thr Phe Glu Glu Ala Ala Leu Leu Val Asn Tyr lle Thr Ala 165 170 175

Tyr Met Val Leu Phe Asp Phe Gly Asn Leu Gln Pro Gly His Ser Val 180 185 190

Leu Val His Met Ala Ala Gly Gly Val Gly Met Ala Ala Val Gln Leu 195 200 205

Cys Arg Thr Val Glu Asn Val Thr Val Phe Gly Thr Ala Ser Ala Ser 210 215 220

Lys His Glu Ala Leu Lys Glu Asn Gly Val Thr His Pro Ile Asp Tyr 225 230 235 240

His Thr Thr Asp Tyr Val Asp Glu IIe Lys Lys IIe Ser Pro Lys Gly 245 250 255

| Val                 | Asp   | lle        | Val<br>260       | Met              | Asp              | Pro              | Leu        | Gly<br>265       | Gly              | Ser              | Asp              | Thr        | A1 a             |                  | Gly              |     |
|---------------------|---|------------|------------------|------------------|------------------|------------------|------------|------------------|------------------|------------------|------------------|------------|------------------|------------------|------------------|-----|
| Tyr                 | Asn   | Leu<br>275 | Leu              | Lys              | Pro              | Met              | Gly<br>280 |                  | Val              | Val              | Thr              | Tyr<br>285 |                  | Met              | Ala              |     |
| Asn                 | Leu<br>290  | Leu        | Thr              | Gly              | Pro              | Lys<br>295       | Arg        | Asn              | Leu              | Met              | Ala<br>300       |            | Ala              | Arg              | Thr              |     |
| Trp<br>305          | Trp   | Asn        | Gin              | Phe              | Ser<br>310       | Val              | Thr        | Ala              | Leu              | Gln<br>315       |                  | Leu        | Gin              | Ala              | Asn<br>320       |     |
| Arg                 | Ala   | Val        | Cys              | Gly<br>325       | Phe              | His              | Leu        | Gly              | Tyr<br>330       |                  | Asp              | Gly        | Glu              | Va I<br>335      |                  |     |
| Leu                 | Val   | Ser        | Gly<br>340       | Val              | Val              | Ala              | Arg        | Leu<br>345       |                  | Ala              | Leu              | Tyr        | Asn<br>350       |                  | Gly              |     |
| His                 | He  | Lys<br>355 | Pro              | His              | He               | Asp              | Ser<br>360 | Val              | Trp              | Pro              | Phe              | G u<br>365 |                  | Val              | Ala              |     |
| Asp                 | Ala<br>370  | Met        | Lys              | Gln              | Met              | GIn<br>375       | Glu        | Lys              | Lys              | Asn              | Va I<br>380      | Gly        | Lys              | Val              | Leu              |     |
| Leu<br>385          | Val   | Pro        | Gly              | Pro              | Glu<br>390       | Lys              | Glu        | Asn              |                  |                  |                  |            |                  |                  |                  |     |
| <21<br><212<br><213 | <pre>&lt;210&gt; 44 &lt;211&gt; 2396 &lt;212&gt; DNA &lt;213&gt; Homo sapiens</pre> |            |                  |                  |                  |                  |            |                  |                  |                  |                  |            |                  |                  |                  |     |
| <221                | > CD  | 0S<br>50)  | (122             | 28)              |                  |                  |            |                  |                  |                  |                  |            |                  |                  |                  |     |
|                     | )> 44<br>.gtgc  |            | ctcc             | atco             | a go             | ctgtg            | gcgct      | cto              | egteg            | ggga             | gtco             | cago       |                  |                  | cc gac<br>er Asp | 58  |
| gag<br>Glu          | aga<br>Arg<br>5   | gag<br>Glu | gta<br>Val       | gcc<br>Ala       | gag<br>Glu       | gca<br>Ala<br>10 | gcg<br>Ala | acc<br>Thr       | ggg<br>Gly       | gaa<br>Glu       | gac<br>Asp<br>15 | gcc<br>Ala | tct<br>Ser       | tcg<br>Ser       | ccg<br>Pro       | 106 |
| cct<br>Pro<br>20    | ccg<br>Pro  | aaa<br>Lys | acc<br>Thr       | gag<br>Glu       | gca<br>Ala<br>25 | gcg<br>Ala       | agc<br>Ser | gac<br>Asp       | ccc<br>Pro       | cag<br>Gln<br>30 | cat<br>His       | ccc<br>Pro | gcg<br>Ala       | gcc<br>Ala       | tcc<br>Ser<br>35 | 154 |
| gaa<br>Glu          | ggg<br>Gly  | gcc<br>Ala | gcc<br>Ala       | gcc<br>Ala<br>40 | gcc<br>Ala       | gcc<br>Ala       | gcc<br>Ala | tcg<br>Ser       | ccg<br>Pro<br>45 | cca<br>Pro       | ctg<br>Leu       | ctg<br>Leu | cgc<br>Arg       | tgc<br>Cys<br>50 | cta<br>Leu       | 202 |
| gtg<br>Val          | ctc<br>Leu  | acc<br>Thr | ggc<br>Gly<br>55 | ttt<br>Phe       | gga<br>Gly       | ggc<br>Gly       | tac<br>Tyr | gac<br>Asp<br>60 | aag<br>Lys       | gtg<br>Val       | aag<br>Lys       | ctg<br>Leu | cag<br>Gln<br>65 | agc<br>Ser       | cgg<br>Arg       | 250 |

| CC                | g gca                | a gog             | r ccc             | c cce             |                   | cct               | ggg               | ccc               | . ססר             | : cas             | rto                | , aca             |                   | Cat               | ctg               | 298 |
|-------------------|----------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|--------------------|-------------------|-------------------|-------------------|-------------------|-----|
| Pro               | Ala                  | Ala<br>70         | Pro               | Pro               | Ala               | Pro               | 75                | Pro               | Gly               | Glr               | i Lei              | Thr<br>80         | Lei               | ı Arg             | g Leu             | 290 |
| cgg<br>Arg        | g gco<br>g Ala<br>85 | ı Cys             | gge<br>Gly        | ctc<br>Leu        | aac<br>Asn        | tto<br>Phe<br>90  | Ala               | gac<br>Asp        | cto<br>Leu        | atg<br>Met        | g gct<br>Ala<br>95 | a Arg             | cag<br>Glr        | g ggg<br>n Gly    | g ctg<br>/ Leu    | 346 |
| tac<br>Tyr<br>100 | Asp                  | cgt<br>Arg        | cto<br>Leu        | ccg<br>Pro        | cct<br>Pro<br>105 | Leu               | cct<br>Pro        | gtc<br>Val        | act<br>Thr        | Ccg<br>Pro        | Gly                | atg<br>Met        | gag<br>Glu        | ggc<br>Gly        | gcg<br>Ala<br>115 | 394 |
| ggt<br>Gly        | gtt<br>Val           | gtg<br>Val        | atc<br>Ile        | gca<br>Ala<br>120 | gtg<br>Val        | ggc<br>Gly        | gag<br>Glu        | gga<br>Gly        | gto<br>Val<br>125 | Ser               | gac<br>Asp         | cgc<br>Arg        | aag<br>Lys        | gca<br>Ala<br>130 | gga<br>Gly        | 442 |
| gac<br>Asp        | cgg<br>Arg           | gtg<br>Val        | atg<br>Met<br>135 | ۷a۱               | ttg<br>Leu        | aac<br>Asn        | cgg<br>Arg        | tca<br>Ser<br>140 | ggg<br>Gly        | atg<br>Met        | tgg<br>Trp         | cag<br>Gln        | gaa<br>Glu<br>145 | Glu               | gtg<br>Val        | 490 |
| act<br>Thr        | gtg<br>Val           | ccc<br>Pro<br>150 | tcg<br>Ser        | gtc<br>Val        | cag<br>G n        | acc<br>Thr        | ttc<br>Phe<br>155 | ctg<br>Leu        | att<br>lle        | cct<br>Pro        | gag<br>Glu         | gcc<br>Ala<br>160 | atg<br>Met        | acc<br>Thr        | ttt<br>Phe        | 538 |
| gag<br>Glu        | gaa<br>Glu<br>165    | Ala               | gct<br>Ala        | gcc<br>Ala        | ttg<br>Leu        | ctc<br>Leu<br>170 | gtc<br>Val        | aat<br>Asn        | tac<br>Tyr        | att<br>lle        | aca<br>Thr<br>175  | gcc<br>Ala        | tac<br>Tyr        | atg<br>Met        | gtc<br>Val        | 586 |
| ctc<br>Leu<br>180 | ttt<br>Phe           | gac<br>Asp        | ttc<br>Phe        | ggc<br>Gly        | aac<br>Asn<br>185 | cta<br>Leu        | cag<br>G n        | cct<br>Pro        | ggc<br>Gly        | cac<br>His<br>190 | agc<br>Ser         | gtc<br>Val        | ttg<br>Leu        | gta<br>Val        | cac<br>His<br>195 | 634 |
| atg<br>Met        | gct<br>Ala           | gca<br>Ala        | ggg<br>Gly        | ggt<br>Gly<br>200 | gtg<br>Val        | ggt<br>Gly        | atg<br>Met        | gct<br>Ala        | gcc<br>Ala<br>205 | gtg<br>Val        | cag<br>Gln         | ctg<br>Leu        | tgc<br>Cys        | cgt<br>Arg<br>210 | aca<br>Thr        | 682 |
| gtg<br>Val        | gag<br>Glu           | aat<br>Asn        | Val               | Thr               | Val               | Phe               | Gly               | Thr               | Ala               | Ser               | Ala                | agc<br>Ser        | Lvs               | His               | gag<br>Glu        | 730 |
| gca<br>Ala        | ctg<br>Leu           | aag<br>Lys<br>230 | gag<br>Glu        | aat<br>Asn        | ggg<br>Gly        | gtc<br>Val        | aca<br>Thr<br>235 | cat<br>His        | ccc<br>Pro        | atc<br>Ile        | gac<br>Asp         | tat<br>Tyr<br>240 | cac<br>His        | acg<br>Thr        | act<br>Thr        | 778 |
| gac<br>Asp        | tac<br>Tyr<br>245    | gtg<br>Val        | gat<br>Asp        | gag<br>Glu        | atc<br>He         | aag<br>Lys<br>250 | aag<br>Lys        | att<br>lle        | tcc<br>Ser        | cct<br>Pro        | aaa<br>Lys<br>255  | gga<br>Gly        | gtg<br>Val        | gac<br>Asp        | att<br>Ile        | 826 |
| gtc<br>Val<br>260 | atg<br>Met           | gac<br>Asp        | cct<br>Pro        | ctg<br>Leu        | ggt<br>Gly<br>265 | ggg<br>Gly        | tca<br>Ser        | gat<br>Asp        | act<br>Thr        | gcc<br>Ala<br>270 | aag<br>Lys         | ggc<br>Gly        | tac<br>Tyr        | aac<br>Asn        | ctc<br>Leu<br>275 | 874 |
| ctg<br>Leu        | aaa<br>Lys           | ccc<br>Pro        | atg<br>Met        | ggc<br>Gly<br>280 | aaa<br>Lys        | gtc<br>Val        | gtc<br>Val        | Thr               | tat<br>Tyr<br>285 | gga<br>Gly        | atg<br>Met         | gcc<br>Ala        | Asn               | ctg<br>Leu<br>290 | ctg<br>Leu        | 922 |
| acg               | ggc                  | ссс               | aaa               | cgg               | aac               | ctg               | atg               | gcc               | ctg               | gcc               | cgg                | aca               | tgg               | tgg               | aat               | 970 |

| Thr               | Gly               | Pro               | Lys<br>295        | Arg               | <b>D</b> r        | Leu               | Met               | Ala<br>300 | Leu               | Ala               | Arg               | Thr               | 30         | Trp               | Asn               |      |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------------|-------------------|-------------------|-------------------|-------------------|------------|-------------------|-------------------|------|
| cag<br>G n        | ttc<br>Phe        | ago<br>Ser<br>310 | gtg<br>Val        | aca<br>Thr        | gct<br>Ala        | ctg<br>Leu        | cag<br>Gln<br>315 | ctg<br>Leu | ctg<br>Leu        | cag<br>Gln        | gcc<br>Ala        | aac<br>Asn<br>320 | cgg<br>Arg | gct<br>Ala        | gtg<br>Val        | 1018 |
| tgt<br>Cys        | ggc<br>Gly<br>325 | tto<br>Phe        | cac<br>His        | ctg<br>Leu        | ggc<br>Gly        | tac<br>Tyr<br>330 | ctg<br>Leu        | gat<br>Asp | ggt<br>Gly        | gag<br>Glu        | gtg<br>Val<br>335 | gag<br>Glu        | ctg<br>Leu | gtc<br>Val        | agt<br>Ser        | 1066 |
| ggt<br>Gly<br>340 | gtg<br>Val        | gtg<br>Val        | gcc<br>Ala        | cgc<br>Arg        | ctc<br>Leu<br>345 | ctg<br>Leu        | gct<br>Ala        | ctg<br>Leu | tac<br>Tyr        | aac<br>Asn<br>350 | cag<br>Gln        | ggc<br>Gly        | cac<br>His | atc<br>lle        | aag<br>Lys<br>355 | 1114 |
| ccc<br>Pro        | cac<br>His        | att<br>lle        | gac<br>Asp        | tca<br>Ser<br>360 | gtc<br>Val        | tgg<br>Trp        | ccc<br>Pro        | ttc<br>Phe | gag<br>Glu<br>365 | aag<br>Lys        | gtg<br>Val        | gct<br>Ala        | gat<br>Asp | gcc<br>Ala<br>370 | atg<br>Met        | 1162 |
|                   |                   |                   | cag<br>Gln<br>375 |                   |                   |                   |                   |            |                   |                   |                   |                   |            |                   |                   | 1210 |
|                   |                   |                   | aag<br>Lys        |                   |                   | tagg              | gcaa              | gt g       | gctg              | gtgag             | да сс             | ctag              | gagad      |                   |                   | 1258 |
| cago              | gaag              | gg                | agaag             | ttgg              | g aa              | gcta              | cgtt              | ctg        | ttgg              | сса               | ccag              | actt              | gc a       | atttc             | agcct             | 1318 |
| ctgt              | cata              | at                | gctct             | gccc              | t cc              | ctcc              | cccg              | aag        | ttct              | ctg               | tggt              | gate              | ac c       | gctc              | tcccc             | 1378 |
| tgcc              | cctc              | cc (              | cgctţ             | cctg              | асс               | tctg              | aaga              | ggt        | tggg              | aag               | tgac              | catt              | tg g       | atgt              | ctggg             | 1438 |
| ccct              | gcca              | ag į              | gcgac             | aggg              | a gg              | gtca              | gagg              | gag        | gccg              | gct               | gctt              | cctg              | cc c       | ссас              | ccttt             | 1498 |
| cccc              | gggc              | ct į              | gctgt             | gctg              | c tt              | ttgt              | gcca              | agg        | ttag              | сса               | gtcc              | cccc              | tg t       | tgtg              | ttcca             | 1558 |
| tgtg              | cttt              | ca d              | cctct             | gcct              | c at              | cttt              | cctc              | ccg        | tccc              | tgc               | cccg              | ccac              | ct c       | ссса              | aagaa             | 1618 |
| ttga              | aacg              | tc a              | agctc             | agga              | t at              | gggg              | ссаа              | tct        | ctgt              | gag               | tcca              | gcat              | gt a       | cctg              | tctct             | 1678 |
| ccct              | agtg              | tc                | ccttc             | agcc              | t gg              | gctg              | асса              | gtg        | cccg              | cct               | ctgg              | gctt              | ga c       | cagt              | tccca             | 1738 |
| atct              | cgtc              | ct                | ctgtc             | ссса              | a ct              | tctt              | aagc              | aca        | attg              | ggc               | ttct              | tcca              | tc t       | ccag              | gtttt             | 1798 |
| ctgc              | catt              | ct t              | taacc             | aagg              | c ag              | cccc              | aagc              | ctc        | ctgg              | gga               | ggca              | gggc              | aa a       | aaca              | ggtgc             | 1858 |
| cctc              | atcg              | tg g              | gtctg             | tgcc              | a tg              | tccc              | gtct              | cta        | tggt              | ggt               | tgag              | gaga              | aa g       | gcgg              | ggaag             | 1918 |
| cttc              | ctca              | gc o              | cttgc             | agat              | a tg              | tgtg              | gcat              | tta        | ctag              | сса               | gagc              | tctg              | aa a       | ggca              | gtgct             | 1978 |
| gtct              | gttt              | ct t              | gtac              | tggg              | a cc              | aaag <sup>.</sup> | taaa              | aat        | ccaa              | gca               | catt              | cccc              | tt g       | cagt <sup>.</sup> | taggg             | 2038 |
| gaggo             | ccct              | ac t              | gcct              | tctc              | a aa              | gcaga             | agag              | gca        | gctt              | atc               | aaac              | tcag              | cc c       | aaaa              | ctctg             | 2098 |
| ttta              | catg              | gg t              | gggg              | agat              | g ga              | gcag              | ggaa              | gta        | caga              | gtg               | ggat              | ggtc              | ag g       | acct              | gggcc             | 2158 |
| attgo             | caac              | ca a              | aatg              | ggga              | c tto             | cctg              | ggta              | ggga       | aggto             | cac               | tccc              | tcta              | ct c       | actga             | agcta             | 2218 |

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Arg Cys Leu Val Leu Thr Gly Phe Gly Gly Tyr Asp Lys Val Lys Leu 50 60

Gin Ser Arg Pro Ala Ala Pro Pro Ala Pro Gly Pro Gly Gin Leu Thr 65 70 75 80

Leu Arg Leu Arg Ala Cys Gly Leu Asn Phe Ala Asp Leu Met Ala Arg 85 90 95

Gln Gly Leu Tyr Asp Arg Leu Pro Pro Leu Pro Val Thr Pro Gly Met 100 105 110

Glu Gly Ala Gly Val Val IIe Ala Val Gly Glu Gly Val Ser Asp Arg 115 120 125

Lys Ala Gly Asp Arg Val Met Val Leu Asn Arg Ser Gly Met Trp Gln 130 140

Glu Glu Val Thr Val Pro Ser Val Gln Thr Phe Leu Ile Pro Glu Ala 145 150 155 160

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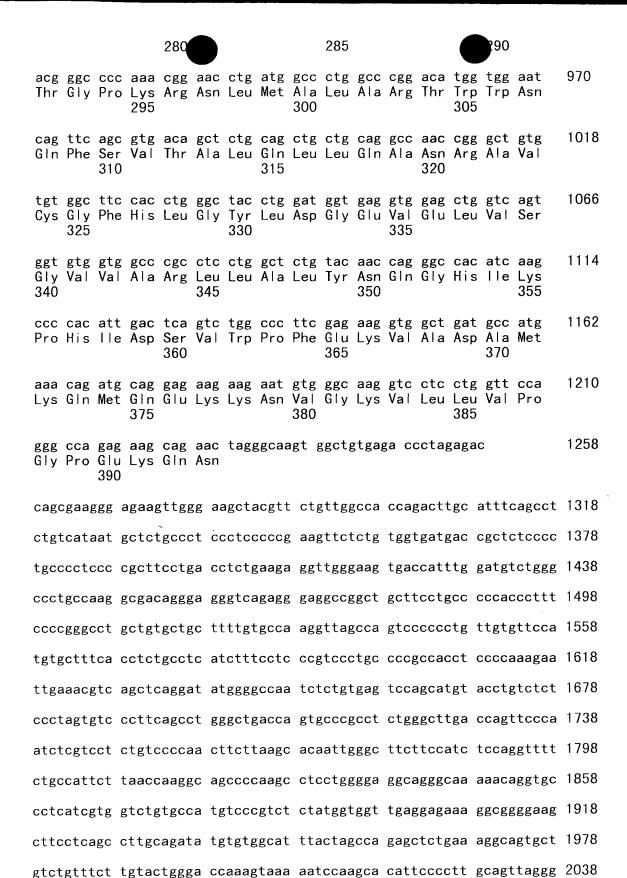
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Cys Arg Thr Val Glu Asn Val Thr Val Phe Gly Thr Ala Ser Ala Ser 210 215 220

Lys His Glu Ala Leu Lys Glu Asn Gly Val Thr His Pro lle Asp Tyr 225 230 235 240

| His                          | Thr             | Thr            | Asp            | 7yı<br>245      | vai              | Asp              | Glu                   | 116        | e Lys<br>250     |                  | s IIe            | e Sei      | r Pr       | o Ly<br>25       | s Gly<br>5       |     |
|------------------------------|-----------------|----------------|----------------|-----------------|------------------|------------------|-----------------------|------------|------------------|------------------|------------------|------------|------------|------------------|------------------|-----|
| Val                          | Asp             | lle            | Val<br>260     | Met             | : Asp            | Pro              | Leu                   | Gly<br>265 | y Gly<br>5       | / Se             | r Asp            | Th:        | A   a      | _                | s Gly            |     |
| Tyr                          | Asn             | Leu<br>275     | Leu            | Lys             | Pro              | Met              | Gly<br>280            | Lys        | s Val            | Va               | l Thr            | Tyr<br>285 |            | y Me             | t Ala            |     |
| Asn                          | Leu<br>290      | Leu            | Thr            | Gly             | Pro              | Lys<br>295       | Arg                   | Asr        | l Lei            | ı Met            | 300              | Leu        | ı Ala      | a Arg            | g Thr            |     |
| Trp<br>305                   | Trp             | Asn            | Gln            | Phe             | Ser<br>310       | Val              | Thr                   | Ala        | ı Leu            | Glr<br>315       | Leu              | Leu        | ı Gir      | n Ala            | a Asn<br>320     |     |
| Arg                          | Ala             | Val            | Cys            | Gly<br>325      | Phe              | His              | Leu                   | Gly        | Tyr<br>330       | Leu              | ı Asp            | Gly        | Glu        | ı Va↓<br>335     | Glu<br>5         |     |
| Leu                          | Val             | Ser            | Gly<br>340     | Val             | Val              | Ala              | Arg                   | Leu<br>345 | Leu              | Ala              | Leu              | Tyr        | Asn<br>350 |                  | n Gly            |     |
| His                          | lle             | Lys<br>355     | Pro            | His             | lle              | Asp              | Ser<br>360            | Val        | Trp              | Pro              | Phe              | Glu<br>365 |            | Val              | Ala              |     |
| Asp                          | Ala<br>370      | Met            | Lys            | Gln             | Met              | GIn<br>375       | Glu                   | Lys        | Lys              | Asn              | Val<br>380       | Gly        | Lys        | Val              | Leu              |     |
| Leu<br>385                   | Val             | Pro            | Gly            | Pro             | Glu<br>390       | Lys              | Gln                   | Asn        |                  |                  |                  |            |            |                  |                  |     |
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| gag a<br>Glu <i>i</i>        | aga<br>Arg<br>5 | gag ;<br>Glu \ | gta ;<br>Val   | gcc<br>Ala      | gag<br>Glu       | gca<br>Ala<br>10 | gcg (<br>Ala          | acc<br>Thr | ggg<br>Gly       | gaa<br>Glu       | gac<br>Asp<br>15 | gcc<br>Ala | tct<br>Ser | tcg<br>Ser       | ccg<br>Pro       | 106 |
| oct d<br>Pro F<br>20         | ocg<br>Pro      | aaa a<br>Lys   | асс į<br>Гhr ( | gag<br>Glu      | gca<br>Ala<br>25 | gcg (<br>Ala (   | agc g<br>Ser <i>l</i> | gac<br>Asp | ccc<br>Pro       | cag<br>Gln<br>30 | cat<br>His       | ccc<br>Pro | gcg<br>Ala | gcc<br>Ala       | tcc<br>Ser<br>35 | 154 |
| gaa g<br>Glu (               | ggg (<br>Gly /  | gcc g<br>Ala A | gcc g<br>Ala A | gcc<br>Na<br>40 | gcc ;<br>Ala ,   | gcc (<br>Ala /   | gcc t<br>Ala S        | cg<br>Ser  | ccg<br>Pro<br>45 | cca<br>Pro       | ctg<br>Leu       | ctg<br>Leu | cgc<br>Arg | tgc<br>Cys<br>50 | cta<br>Leu       | 202 |

| gtg<br>Val        | ctc<br>Leu | acc<br>Thr        | ggc<br>Gly<br>55 | ttt<br>Phe        | a<br>GI y         | ggc<br>Gly | tac<br>Tyr        | gac<br>Asp<br>60 | aag<br>Lys        | gtg<br>Val        | aag<br>Lys | ctg<br>Leu        | G I II<br>65 | agc<br>Ser        | cgg<br>Arg        | 250 |
|-------------------|------------|-------------------|------------------|-------------------|-------------------|------------|-------------------|------------------|-------------------|-------------------|------------|-------------------|--------------|-------------------|-------------------|-----|
|                   |            |                   |                  |                   |                   |            |                   |                  |                   |                   |            | acg<br>Thr<br>80  |              |                   |                   | 298 |
|                   |            |                   |                  |                   |                   |            |                   |                  |                   |                   |            | agg<br>Arg        |              |                   |                   | 346 |
|                   |            |                   |                  |                   |                   |            |                   |                  |                   |                   |            | atg<br>Met        |              |                   |                   | 394 |
|                   |            |                   |                  |                   |                   |            |                   |                  |                   |                   |            | cgc<br>Arg        |              |                   |                   | 442 |
|                   |            |                   |                  |                   |                   |            |                   |                  |                   |                   |            | cag<br>Gln        |              |                   |                   | 490 |
|                   |            |                   |                  |                   |                   |            |                   |                  |                   |                   |            | gcc<br>Ala<br>160 |              |                   |                   | 538 |
|                   |            |                   |                  |                   |                   |            |                   |                  |                   |                   |            | gcc<br>Ala        |              |                   |                   | 586 |
|                   |            |                   |                  |                   |                   |            |                   |                  |                   |                   |            | gtc<br>Val        |              |                   |                   | 634 |
| atg<br>Met        | gct<br>Ala | gca<br>Ala        | ggg<br>Gly       | ggt<br>Gly<br>200 | gtg<br>Val        | ggt<br>Gly | atg<br>Met        | Ala              | gcc<br>Ala<br>205 | gtg<br>Val        | cag<br>Gln | ctg<br>Leu        | tgc<br>Cys   | cgt<br>Arg<br>210 | aca<br>Thr        | 682 |
|                   |            |                   |                  |                   |                   |            |                   |                  |                   |                   |            | agc<br>Ser        |              |                   |                   | 730 |
| gca<br>Ala        | ctg<br>Leu | aag<br>Lys<br>230 | gag<br>Glu       | aat<br>Asn        | ggg<br>Gly        | gtc<br>Val | aca<br>Thr<br>235 | cat<br>His       | ccc<br>Pro        | atc<br>lle        | gac<br>Asp | tat<br>Tyr<br>240 | cac<br>His   | acg<br>Thr        | act<br>Thr        | 778 |
|                   |            |                   |                  |                   |                   |            |                   |                  |                   |                   |            | gga<br>Gly        |              |                   |                   | 826 |
| gtc<br>Val<br>260 | atg<br>Met | gac<br>Asp        | cct<br>Pro       | ctg<br>Leu        | ggt<br>Gly<br>265 | ggg<br>Gly | tca<br>Ser        | gat<br>Asp       | act<br>Thr        | gcc<br>Ala<br>270 | aag<br>Lys | ggc<br>Gly        | tac<br>Tyr   | aac<br>Asn        | ctc<br>Leu<br>275 | 874 |
|                   |            |                   |                  |                   |                   |            |                   |                  |                   |                   |            | gcc<br>Ala        |              |                   |                   | 922 |



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| tta acg gac acg cag aaa att gga atg gga tta aca gga ttt gga gtg 16<br>Leu Thr Asp Thr Gin Lys ile Gly Met Gly Leu Thr Gly Phe Gly Val<br>5 10 15      | 66       |
|---|----------|
| 20 25 30 Sala Leu Leu 25  | 14       |
| gct att gga aat gtt tta ttt gta gcc ggc ttg gct ttt gta att ggt 26<br>Ala lle Gly Asn Val Leu Phe Val Ala Gly Leu Ala Phe Val lle Gly<br>40 45 50     | 32       |
| tta gaa aga aca ttc aga ttc ttc ttc caa aaa cat aaa atg aaa gct 31<br>Leu Glu Arg Thr Phe Arg Phe Phe Phe Gln Lys His Lys Met Lys Ala<br>55 60 65     | 0        |
| aca ggt ttt ttt ctg ggt ggt gta ttt gta gtc ctt att ggt tgg cct 358<br>Thr Gly Phe Phe Leu Gly Gly Val Phe Val Val Leu Ile Gly Trp Pro<br>70 75 80    | 8        |
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Ala Leu Leu Leu Asn Asp Leu Lys Lys His Thr Ala Asp Glu Asn Pro 50 55 60 ,

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Thr His IIe Asn Glu Asp Lys Arg Lys Thr Glu Ala Gln Lys Gln IIe 85 90 95

Phe Asp Val Val Tyr Glu Val Asp Gly Cys Pro Ala Asn Leu Leu Ser 100 - 105 110

Ser His Arg Ser Leu Val Gln Arg Val Glu Thr lle Ser Leu Gly Glu 115 120 125

His Pro Cys Asp Arg Gly Glu Gln Val Thr Leu Phe Leu Phe Asn Asp 130 135 140

Cys Leu Glu IIe Ala Arg Lys Arg His Lys Val IIe Gly Thr Phe Arg 145 150 155 160

Ser Pro His Gly Gln Thr Arg Pro Pro Ala Ser Leu Lys His Ile His 165 170 175

Leu Met Pro Leu Ser Gin Ile Lys Lys Val Leu Asp Ile Arg Glu Thr 180 185 190

Glu Asp Cys His Asn Ala Phe Ala Leu Leu Val Arg Pro Pro Thr Glu 195 200 205

Gin Ala Asn Val Leu Leu Ser Phe Gin Met Thr Ser Asp Giu Leu Pro 210 215 220

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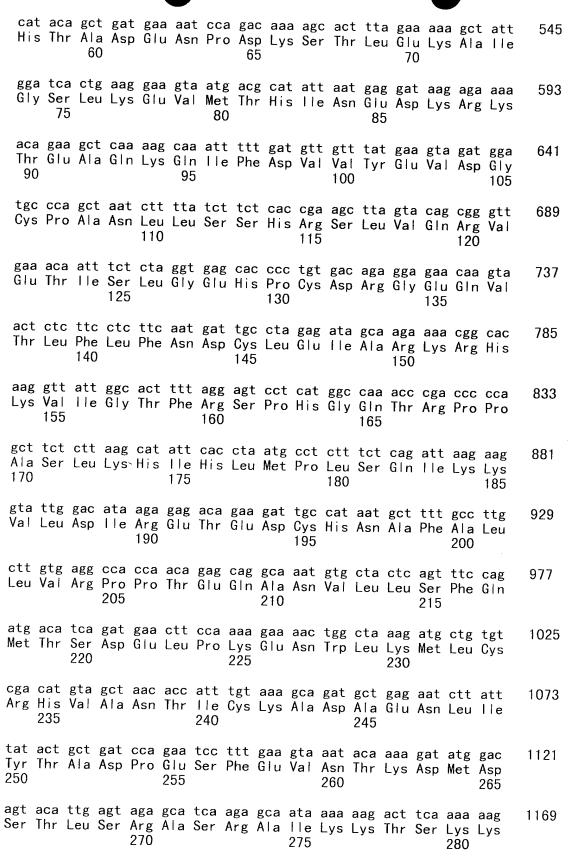
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accetecett tgtaaactte tttgaa atg age aag gaa aca att att aaa tgt 353 Met Ser Lys Glu Thr lle lle Lys Cys 1 5

gaa aaa cag aaa cca aga ttt cat gct ttt ctc aag ata aac caa gca 401 Glu Lys Gin Lys Pro Arg Phe His Ala Phe Leu Lys Ile Asn Gin Ala 10 15 20 25

aaa cca gaa tgt gga cgg cag agc ctt gtt gaa ctt ctt atc cga cca 449 Lys Pro Glu Cys Gly Arg Gln Ser Leu Val Glu Leu Leu Ile Arg Pro 30 35 40

gta cag agg tta ccc agt gtt gca tta ctt tta aat gat ctt aag aag (497 Val Gln Arg Leu Pro Ser Val Ala Leu Leu Leu Asn Asp Leu Lys Lys 

| gtt aca aga gca ttc  | 7 |
|--|---|
| agg gct ctt atg aca tcc cac ggc tca gtg gag gga aga agt cct tcc 1269<br>Arg Ala Leu Met Thr Ser His Gly Ser Val Glu Gly Arg Ser Pro Ser<br>300 305 310                 | 5 |
| agc aat gat aag cat gta atg agt cgt ctt tct agc aca tca tca tta 1313<br>Ser Asn Asp Lys His Val Met Ser Arg Leu Ser Ser Thr Ser Ser Leu<br>315 320 325                 | 3 |
| gca ggt atc cct tct ccc tcc ctt gtc agc ctt cct tcc ttc ttt gaa 136 <sup>-</sup><br>Ala Gly Ile Pro Ser Pro Ser Leu Val Ser Leu Pro Ser Phe Phe Glu<br>330 335 340 345 | I |
| agg aga agt cat acg tta agt aga tct aca act cat ttg ata 1403<br>Arg Arg Ser His Thr Leu Ser Arg Ser Thr Thr His Leu Ile<br>350 355                                     | 3 |
| tgaagcgtta ccaaaatctt aaattataga aatgtataga cacctcatac tcaaataaga 1463   | } |
| aactgactta aatggtactt gtaattagca cttggtgaaa gctggaagga agataaataa 1523   | } |
| cactaaacta tgctatttga tttttcttct tgaaagagta aggtttacct gttacatttt 1583   | } |
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| tgtcattcaa aggccaataa tttaagttgc tatcagctga tattagtagc tttgcaaccc 1703   | } |
| tgatagagta aataaatttt atgggcgggt gccaaatact gctgtgaatc tatttgtata 1763   | } |
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| ttcacatgtg cagtttgaag tatttaaata accactcctt tcacagttta ttttcttctc 1943   |   |
| aagcgttttc aagatctagc atgtggattt taaaagattt gccctcatta acaagaataa 2003   |   |
| catttaaagg agattgtttc aaaatatttt tgcaaattga gataaggaca gaaagattga 2063   |   |
| gaaacattgt atattttgca aaaacaagat gtttgtagct gtttcagaga gagtacggta 2123   |   |
| tatttatggt aattttatcc actagcaaat cttgatttag tttgatagtg tgtggaattt 2183   |   |
| tattttgaag gataagacca tgggaaaatt gtggtaaaga ctgtttgtac ccttcatgaa 2243   |   |
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<211> 883

<212> PRT

<213> Homo sapiens

<400> 51

Met Ala Glu Asn Ser Val Leu Thr Ser Thr Thr Gly Arg Thr Ser Leu

Ala Asp Ser Ser lie Phe Asp Ser Lys Val Thr Glu lie Ser Lys Glu

Asn Leu Leu lle Gly Ser Thr Ser Tyr Val Glu Glu Glu Met Pro Gln

lle Glu Thr Arg Val Ile Leu Val Gln Glu Ala Gly Lys Gln Glu Glu

Leu Thr Lys Ala Leu Lys Asp lle Lys Val Gly Phe Val Lys Met Glu

Ser Val Glu Glu Phe Glu Gly Leu Asp Ser Pro Glu Phe Glu Asn Val

Phe Val Val Thr Asp Phe Gln Asp Ser Val Phe Asn Asp Leu Tyr Lys 100

Ala Asp Cys Arg Val Ile Gly Pro Pro Val Val Leu Asn Cys Ser Gln

Lys Gly Glu Pro Leu Pro Phe Ser Cys Arg Pro Leu Tyr Cys Thr Ser

Met Met Asn Leu Val Leu Cys Phe Thr Gly Phe Arg Lys Lys Glu Glu 145

Leu Val Arg Leu Val Thr Leu Val His His Met Gly Gly Val lle Arg

Lys Asp Phe Asn Ser Lys Val Thr His Leu Val Ala Asn Cys Thr Gln

Gly Glu Lys Phe Arg Val Ala Val Ser Leu Gly Thr Pro Ile Met Lys

Pro Glu Trp Ile Tyr Lys Ala Trp Glu Arg Arg Asn Glu Gln Asp Phe 215

Tyr Ala Ala Val Asp Asp Phe Arg Asn Glu Phe Lys Val Pro Pro Phe 225

Gln Asp Cys lle Phe Ser Phe Leu Gly Phe Ser Asp Glu Glu Lys Thr 245 250



Gly Asp Glu Arg Cys Thr His Leu Val Val Glu Glu Asn 11e Val Lys 275 280 285

Asp Leu Pro Phe Glu Pro Ser Lys Lys Leu Tyr Val Val Lys Gln Glu 290 295 300

Trp Phe Trp Gly Ser lle Gln Met Asp Ala Arg Ala Gly Glu Thr Met 305 310 315 320

Tyr Leu Tyr Glu Lys Ala Asn Thr Pro Glu Leu Lys Lys Ser Val Ser 325 330 335

Met Leu Ser Leu Asn Thr Pro Asn Ser Asn Arg Lys Arg Arg Arg Leu 340 350

Lys Glu Thr Leu Ala Gin Leu Ser Arg Asp Thr Asp Val Ser Pro Phe 355 360 365

Pro Pro Arg Lys Arg Pro Ser Ala Glu His Ser Leu Ser Ile Gly Ser 370 380

Leu Leu Asp lie Ser Asn Thr Pro Glu Ser Ser lie Asn Tyr Gly Asp 385 390 395 400

Thr Pro Lys Ser Cys Thr Lys Ser Ser Lys Ser Ser Thr Pro Val Pro 405 410 415

Ser Lys Gln Ser Ala Arg Trp Gln Val Ala Lys Glu Leu Tyr Gln Thr 420 430

Glu Ser Asn Tyr Val Asn Ile Leu Ala Thr Ile Ile Gln Leu Phe Gln 435 440 445

Val Pro Leu Glu Glu Glu Gly Gln Arg Gly Gly Pro Ile Leu Ala Pro 450 455 460

Glu Glu IIe Lys Thr IIe Phe Gly Ser IIe Pro Asp IIe Phe Asp Val 465 470 475 480

His Thr Lys IIe Lys Asp Asp Leu Glu Asp Leu IIe Val Asn Trp Asp 485 490 495

Glu Ser Lys Ser lle Gly Asp lle Phe Leu Lys Tyr Ser Lys Asp Leu 500 505 510

Val Lys Thr Tyr Pro Pro Phe Val Asn Phe Phe Glu Met Ser Lys Glu 515 520 525

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Lys lle Asn Gln Ala Lys Pro Glu Cys Gly Arg Gln Ser Leu Val Glu 545 550 560

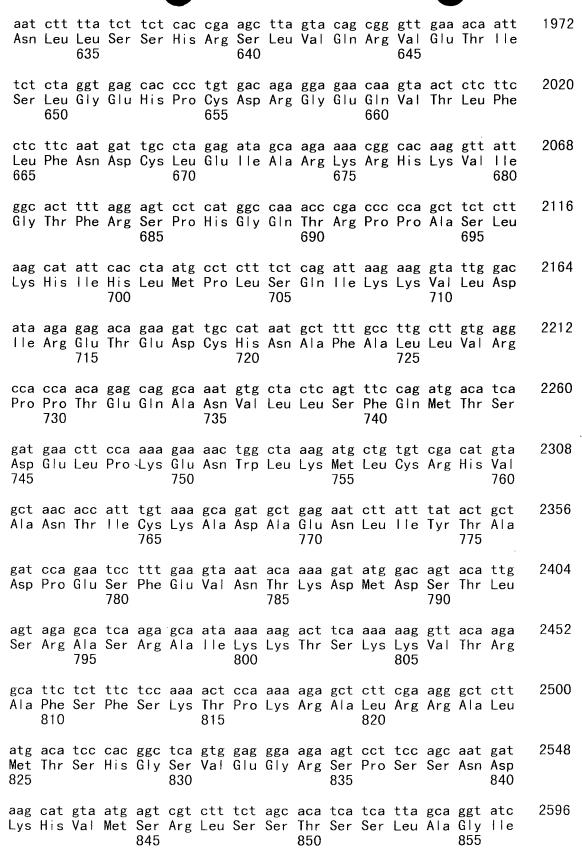
Leu Leu IIe Arg Pro III Gin Arg Leu Pro Ser Val Ala L Leu Leu 575 Asn Asp Leu Lys Lys His Thr Ala Asp Glu Asn Pro Asp Lys Ser Thr 585 Leu Glu Lys Ala Ile Gly Ser Leu Lys Glu Val Met Thr His lle Asn 600 Glu Asp Lys Arg Lys Thr Glu Ala Gln Lys Gln Ile Phe Asp Val Val Tyr Glu Val Asp Gly Cys Pro Ala Asn Leu Leu Ser Ser His Arg Ser Leu Val Gln Arg Val Glu Thr lle Ser Leu Gly Glu His Pro Cys Asp Arg Gly Glu Gln Val Thr Leu Phe Leu Phe Asn Asp Cys Leu Glu lle 665 Ala Arg Lys Arg His Lys Val IIe Gly Thr Phe Arg Ser Pro His Gly 680 GIn Thr Arg Pro Pro Ala Ser Leu Lys His Ile His Leu Met Pro Leu 695 Ser Gln lle Lys Lys Val Leu Asp lle Arg Glu Thr Glu Asp Cys His 720 Asn Ala Phe Ala Leu Leu Val Arg Pro Pro Thr Glu Gln Ala Asn Val Leu Leu Ser Phe Gin Met Thr Ser Asp Giu Leu Pro Lys Giu Asn Trp 745 Leu Lys Met Leu Cys Arg His Val Ala Asn Thr Ile Cys Lys Ala Asp 755 Ala Glu Asn Leu Ile Tyr Thr Ala Asp Pro Glu Ser Phe Glu Val Asn Thr Lys Asp Met Asp Ser Thr Leu Ser Arg Ala Ser Arg Ala Ile Lys Lys Thr Ser Lys Lys Val Thr Arg Ala Phe Ser Phe Ser Lys Thr Pro Lys Arg Ala Leu Arg Arg Ala Leu Met Thr Ser His Gly Ser Val Glu 825 Gly Arg Ser Pro Ser Ser Asn Asp Lys His Val Met Ser Arg Leu Ser Ser Thr Ser Ser Leu Ala Gly IIe Pro Ser Pro Ser Leu Val Ser Leu 850 855 860 Pro Ser Phe Phe Glu Arg Arg Ser His Thr Leu Ser Arg Ser Thr Thr

His Leu IIe

| <210> 52<br><211> 3910<br><212> DNA<br><213> Homo sapiens                                |                  |            |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |     |
|--|------------------|------------|------------|------------|-------------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|-------------------|-----|
| <220><br><221> CDS<br><222> (29) (2677)  |                  |            |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |     |
| <pre>&lt;400&gt; 52 agagtgctga tttagaagaa tacaaatc atg gct gaa aat agt gta tta aca</pre> |                  |            |            |            |                   |            |            |            |            |                   |            |            |            |            | 52                |     |
|  | act<br>Thr<br>10 |            |            |            |                   |            |            |            |            |                   |            |            |            |            |                   | 100 |
|  | gtt<br>Val       |            |            |            |                   |            |            |            |            |                   |            |            |            |            |                   | 148 |
|  | gta<br>Val       |            |            |            |                   |            |            |            |            |                   |            |            |            |            |                   | 196 |
|  | gaa<br>Glu       |            |            |            |                   |            |            |            |            |                   |            |            |            |            |                   | 244 |
|  | gtg<br>Val       |            |            |            |                   |            |            |            |            |                   |            |            |            |            |                   | 292 |
|  | tct<br>Ser<br>90 |            |            |            |                   |            |            |            |            |                   |            |            |            |            |                   | 340 |
| tct<br>Ser<br>105  | gtc<br>Val       | ttt<br>Phe | aat<br>Asn | gac<br>Asp | ctc<br>Leu<br>110 | tac<br>Tyr | aag<br>Lys | gct<br>Ala | gat<br>Asp | tgt<br>Cys<br>115 | aga<br>Arg | gtt<br>Val | att<br>lle | gga<br>Gly | cca<br>Pro<br>120 | 388 |
|  | gtt<br>Val       |            |            |            |                   |            |            |            |            |                   |            |            |            |            |                   | 436 |
|  | cgc<br>Arg       |            |            |            |                   |            |            |            |            |                   |            |            |            |            |                   | 484 |
| act<br>Thr   | gga<br>Gly       | ttt<br>Phe | agg<br>Arg | aaa<br>Lys | aaa<br>Lys        | gaa<br>Glu | gaa<br>Glu | cta<br>Leu | gtc<br>Val | agg<br>Arg        | ttg<br>Leu | gtg<br>Val | aca<br>Thr | ttg<br>Leu | gtc<br>Val        | 532 |

| cat cac a<br>His His M<br>170     | tg ggt gg<br>et Gly Gl               | a gtt att<br>y Val Ile<br>175 | Hrg Ly                    | a gac tt<br>s Asp Ph          | t aat tca a<br>e Asn Ser L<br>180 | aaa gtt aca<br>.ys Val Thr      | 580  |
|-----------------------------------|--------------------------------------|-------------------------------|---------------------------|-------------------------------|-----------------------------------|---------------------------------|------|
| cat ttg g<br>His Leu Va<br>185    | tg gca aa <sup>.</sup><br>al Ala Ası | t tgt aca<br>n Cys Thr<br>190 | caa gg<br>Gin Gi          | a gaa aa<br>y Glu Ly:<br>19   | a ttc agg g<br>s Phe Arg V<br>5   | tt gct gtg<br>al Ala Val<br>200 | 628  |
| agt cta gg<br>Ser Leu G           | gt act cca<br>ly Thr Pro<br>205      | , ite met                     | aag cca<br>Lys Pro        | gaa tgg<br>Glu Trp<br>210     | g att tat a<br>Dille Tyr L        | aa gct tgg<br>ys Ala Trp<br>215 | 676  |
| gaa agg cg<br>Glu Arg Ar          | gg aat gaa<br>g Asn Glu<br>220       | cag gat<br>Gln Asp            | ttc tat<br>Phe Tyr<br>225 | ' Ala Ala                     | a gtt gat g<br>a Val Asp A<br>2   | ac ttt aga<br>sp Phe Arg<br>30  | 724  |
| aat gaa tt<br>Asn Glu Ph<br>23    | c cys var                            | cct cca<br>Pro Pro            | ttt caa<br>Phe Gin<br>240 | gat tgt<br>Asp Cys            | att ttt ag<br>ile Phe Se<br>245   | gt ttc ctg<br>er Phe Leu        | 772  |
| gga ttt tc<br>Gly Phe Se<br>250   | a gat gaa<br>r Asp Glu               | gag aaa<br>Glu Lys<br>255     | acc aat<br>Thr Asn        | atg gaa<br>Met Glu            | gaa atg ad<br>Glu Met Th<br>260   | et gaa atg<br>or Glu Met        | 820  |
| caa gga gg<br>Gin Gly Gly<br>265  | t aaa tat<br>y Lys Tyr               | tta ccg<br>Leu Pro<br>270     | ctt gga<br>Leu Gly        | gat gaa<br>Asp Glu<br>275     | aga tgc ac<br>Arg Cys Th          | t cac ctt<br>r His Leu<br>280   | 868  |
| gta gtt gaa<br>Val Val Glu        | a gag aat<br>u Glu`Asn<br>285        | ata gta a<br>Ile Val I        | aaa gat<br>Lys Asp        | ctt ccc<br>Leu Pro<br>290     | ttt gaa cc<br>Phe Glu Pr          | t tca aag<br>o Ser Lys<br>295   | 916  |
| aaa ctt tat<br>Lys Leu Tyr        | 300                                  | Lys Gill (                    | 305                       | Phe Irp                       | Gly Ser III<br>310                | e Gin Met<br>)                  | 964  |
| gat gcc cga<br>Asp Ala Arg<br>315 | nia uly                              | did inr W                     | itg tat<br>let Tyr<br>20  | tta tat<br>Leu Tyr            | gaa aag gca<br>Glu Lys Ala<br>325 | a aat act<br>a Asn Thr          | 1012 |
| cct gag ctc<br>Pro Glu Leu<br>330 | aag aaa<br>Lys Lys S                 | tca gtg t<br>Ser Val S<br>335 | ca atg<br>er Met I        | Leu Ser I                     | cta aat acc<br>Leu Asn Thr<br>340 | cct aac<br>Pro Asn              | 1060 |
| agc aat cgc<br>Ser Asn Arg<br>345 | Lys Alg                              | ogt ogt t<br>Arg Arg L<br>850 | ta aaa g<br>eu Lys (      | gaa aca d<br>Glu Thr L<br>355 | ctt gct cag<br>_eu Ala Gin        | ctt tca<br>Leu Ser<br>360       | 1108 |
| aga gat aca<br>Arg Asp Thr        | gac gtg t<br>Asp Val S<br>365        | ca cca t<br>er Pro Pl         | ne Pro F                  | occ cgt a<br>Pro Arg L<br>370 | aag cgc cca<br>ys Arg Pro         | tca gct<br>Ser Ala<br>375       | 1156 |
| gag cat tcc<br>Glu His Ser        | ctt tcc a<br>Leu Ser I<br>380        | ta ggg to<br>le Gly Se        | er Leu L<br>385           | ta gat a<br>eu Asp I          | tc tcc aac<br>le Ser Asn<br>390   | aca cca<br>Thr Pro              | 1204 |

|                   |                    |                     |                       |                            |                       |                       |                       |                   |                   |                     |                     |                     | _                 |                    |                       |      |
|-------------------|--------------------|---------------------|-----------------------|----------------------------|-----------------------|-----------------------|-----------------------|-------------------|-------------------|---------------------|---------------------|---------------------|-------------------|--------------------|-----------------------|------|
| ga;<br>Gli        | g tc<br>u Se       | t ag<br>r Se<br>39  | rii                   | t aa<br>e Asi              | 1 ly                  | t gga<br>r Gly        | a gad<br>/ Asi<br>400 | o Ini             | c cc<br>r Pr      | a aag<br>o Lys      | g tc<br>s Se        | t tg<br>r Cys<br>40 | s Th              | aa<br>r Ly         | g tct<br>s Ser        | 1252 |
| tci<br>Sei        | t aa<br>r Ly<br>41 | s Se                | c tc<br>r Se          | c ac <sup>.</sup><br>r Thi | t cca                 | a gtt<br>o Val<br>415 | Pro                   | t toa<br>Sei      | a aag             | g cag<br>s Gli      | g tc<br>1 Se<br>420 | r Ala               | a ag              | g tg<br>g Tr       | g caa<br>p Gln        | 1300 |
| gt1<br>Va<br>425  | A L                | a aa<br>a Ly        | a ga<br>s Gl          | g cti<br>u Lei             | t tat<br>u Tyr<br>430 | r Gir                 | act<br>Thr            | gaa<br>Glu        | a agt             | t aat<br>Asr<br>435 | י Tyı               | t gti<br>r Va       | aa<br>Ası         | t ata              | a ttg<br>e Leu<br>440 | 1348 |
| gca<br>Ala        | a aca              | a at                | t at<br>e IIo         | t cag<br>e Gir<br>445      | ı Lei                 | a ttt<br>ı Phe        | caa<br>Glr            | agta<br>Val       | Pro<br>450        | ) Leι               | g gaa<br>u Glu      | a gag<br>u Glu      | g gaa<br>i Gli    | gga<br>u Gly<br>45 | a caa<br>y Gin        | 1396 |
| cgt<br>Arg        | ggt<br>Gly         | t gga               | a cct<br>y Pro<br>460 | o He                       | : ctt<br>: Leu        | gca<br>Ala            | cca<br>Pro            | gag<br>Glu<br>465 | Gli               | g att<br>i lle      | aag<br>Lys          | g act<br>Thr        | att<br>11e<br>470 | Phe                | t ggt<br>e Gly        | 1444 |
| ago<br>Ser        | ato<br>Ile         | e cca<br>Pro<br>475 | o Asp                 | ato<br>lle                 | ttt<br>Phe            | gat<br>Asp            | gta<br>Val<br>480     | His               | act<br>Thr        | aag<br>Lys          | ata                 | aag<br>Lys<br>485   | Asp               | gat<br>Asp         | ctt<br>Leu            | 1492 |
| gaa<br>Glu        | gac<br>Asp<br>490  | Let                 | ata<br>u lle          | gtt<br>Val                 | aat<br>Asn            | tgg<br>Trp<br>495     | gat<br>Asp            | gag<br>Glu        | agc<br>Ser        | aaa<br>Lys          | ago<br>Ser<br>500   | lle                 | ggt<br>Gly        | gac<br>Asp         | att                   | 1540 |
| ttt<br>Phe<br>505 | ctg<br>Leu         | Lys                 | tat<br>Tyr            | tca<br>Ser                 | aaa<br>Lys<br>510     | gat<br>Asp            | ttg<br>Leu            | gta<br>Val        | aaa<br>Lys        | acc<br>Thr<br>515   | tac<br>Tyr          | cct<br>Pro          | ccc<br>Pro        | ttt<br>Phe         | gta<br>Val<br>520     | 1588 |
| aac<br>Asn        | ttc<br>Phe         | ttt<br>Phe          | gaa<br>Glu            | atg<br>Met<br>525          | agc<br>Ser            | aag<br>Lys            | gaa<br>Glu            | aca<br>Thr        | att<br>lie<br>530 | att                 | aaa<br>Lys          | tgt<br>Cys          | gaa<br>Glu        | aaa<br>Lys<br>535  | cag<br>Gln            | 1636 |
| aaa<br>Lys        | cca<br>Pro         | aga<br>Arg          | Phe                   | cat<br>His                 | Ala                   | ttt<br>Phe            | Leu                   | Lys               | He                | aac<br>Asn          | caa<br>Gln          | gca<br>Ala          | aaa<br>Lys<br>550 | cca<br>Pro         | gaa<br>Glu            | 1684 |
| tgt<br>Cys        | gga<br>Gly         | cgg<br>Arg<br>555   | cag<br>G n            | agc<br>Ser                 | ctt<br>Leu            | gtt<br>Va!            | gaa<br>Glu<br>560     | ctt<br>Leu        | ctt<br>Leu        | atc<br>He           | cga<br>Arg          | cca<br>Pro<br>565   | gta<br>Val        | cag<br>G n         | agg<br>Arg            | 1732 |
| tta<br>Leu        | ccc<br>Pro<br>570  | agt<br>Ser          | gtt<br>Va!            | gca<br>Ala                 | tta<br>Leu            | ctt<br>Leu<br>575     | tta<br>Leu            | aat<br>Asn        | gat<br>Asp        | ctt<br>Leu          | aag<br>Lys<br>580   | aag<br>Lys          | cat<br>His        | aca<br>Thr         | gct<br>Ala            | 1780 |
| gat<br>Asp<br>585 | gaa<br>Glu         | aat<br>Asn          | cca<br>Pro            | gac<br>Asp                 | aaa<br>Lys<br>590     | agc<br>Ser            | act<br>Thr            | tta<br>Leu        | gaa<br>Glu        | aaa<br>Lys<br>595   | gct<br>Ala          | att<br>lle          | gga<br>Gly        | tca<br>Ser         | ctg<br>Leu<br>600     | 1828 |
| aag<br>Lys        | gaa<br>Glu         | gta<br>Val          | atg<br>Met            | acg<br>Thr<br>605          | cat<br>His            | att .<br>Ile .        | aat<br>Asn            | Glu               | gat<br>Asp<br>610 | aag<br>Lys          | aga<br>Arg          | aaa<br>Lys          | Thr               | gaa<br>Glu<br>615  | gct<br>Ala            | 1876 |
| caa<br>Gln        | aag<br>Lys         | caa<br>Gln          | att<br>lle            | ttt<br>Phe                 | gat<br>Asp            | gtt (<br>Val V        | gtt<br>Val            | Tyr               | gaa<br>Glu<br>133 | gta<br>Val          | gat<br>Asp          | gga<br>Gly          | tgc<br>Cys        | cca<br>Pro         | gct<br>Ala            | 1924 |



2644

cat acg tta agt aga tct aca act cat ttg ata tgaagcgtta ccaaaatctt 2697 His Thr Leu Ser Arg Ser Thr Thr His Leu Ile 875 880

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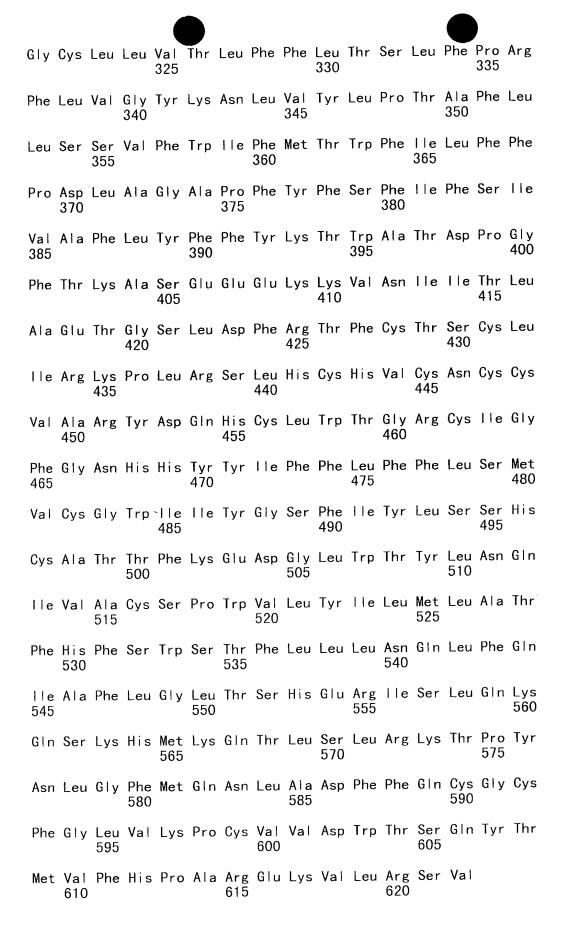
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<sup>&</sup>lt;211> 622

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

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- Lys Glu Leu Ala Asn Ala Arg Glu Ala Leu Pro Leu lle Glu Asp Ser 35 40 45
- Ser Asn Cys Asp lle Val Lys Ala Thr Gln Tyr Gly lle Phe Glu Arg 50 55 60
- Cys Lys Glu Leu Val Glu Ala Gly Tyr Asp Val Arg Gln Pro Asp Lys 65 70 75 80
- Glu Asn Val Ser Leu Leu His Trp Ala Ala Ile Asn Asn Arg Leu Asp 85 90 95
- Leu Val Lys Phe Tyr lle Ser Lys Gly Ala Val Val Asp Gln Leu Gly
  100 105 110
- Gly Asp Leu Asn Ser Thr Pro Leu His Trp Ala Ile Arg Gln Gly His 115 120 125
- Leu Pro Met Val IIe Leu Leu Leu Gln His Gly Ala Asp Pro Thr Leu 130 135 140
- lle Asp Gly Glu Gly Phe Ser Ser lle His Leu Ala Val Leu Phe Gln 145 150 155 160
- His Met Pro IIe IIe Ala Tyr Leu IIe Ser Lys Gly Gln Ser Val Asn 165 170 175
- Met Thr Asp Val Asn Gly Gln Thr Pro Leu Met Leu Ser Ala His Lys 180 185 190
- Val lle Gly Pro Glu Pro Thr Gly Phe Leu Leu Lys Phe Asn Pro Ser 195 200 205
- Leu Asn Val Val Asp Lys lle His Gln Asn Thr Pro Leu His Trp Ala 210 215 220
- Val Ala Ala Gly Asn Val Asn Ala Val Asp Lys Leu Leu Glu Ala Gly 225 230 235 240
- Ser Ser Leu Asp IIe Gln Asn Val Lys Gly Glu Thr Pro Leu Asp Met 245 250 255
- Ala Leu Gln Asn Lys Asn Gln Leu Ile Ile His Met Leu Lys Thr Glu 260 265 270
- Ala Lys Met Arg Ala Asn Gln Lys Phe Arg Leu Trp Arg Trp Leu Gln 275 280 285
- Lys Cys Glu Leu Phe Leu Leu Leu Met Leu Ser Val lle Thr Met Trp 290 295 300
- Ala lle Gly Tyr lle Leu Asp Phe Asn Ser Asp Ser Trp Leu Leu Lys 305 310 315 320



| <210> 54<br><211> 2426<br><212> DNA<br><213> Homo | sapiens                       |                          |                           |                           |                           |                           |                       |          |
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| <220><br><221> CDS<br><222> (104)                 | (1969)                        |                          |                           |                           |                           |                           |                       |          |
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| gctacttgcc  | tagtagcct                     | c agccgc                 | ctgtg gg                  | ctcctggg                  |                           | gag ggg<br>Glu Gly        |                       | <u>,</u> |
| ggg ctg ggc<br>Gly Leu Gly<br>5                   | tcg cag<br>Ser Gln            | tgc agg<br>Cys Arg<br>10 | aat cac<br>Asn His        | agc cat<br>Ser His<br>15  | ggc ccc<br>Gly Pro        | cac cct<br>His Pro        | cca 163<br>Pro<br>20  | )        |
| gga ttt ggt<br>Gly Phe Gly                        | cga tat i<br>Arg Tyr (<br>25  | ggc atc<br>Gly lle       | tgt gca<br>Cys Ala        | cat gaa<br>His Glu<br>30  | aac aaa<br>Asn Lys        | gaa ctt<br>Glu Leu<br>35  | gcc 211<br>Ala        |          |
| aat gca aga<br>Asn Ala Arg                        | gaa gct o<br>Glu Ala l<br>40  | ctt cct<br>Leu Pro       | ctt ata<br>Leu lle<br>45  | gag gac<br>Glu Asp        | tct agt<br>Ser Ser        | aac tgt<br>Asn Cys<br>50  | gac 259<br>Asp        |          |
| att gtc aaa<br>IIe Val Lys<br>55                  | Ala Thr (                     | caa tac<br>Gln Tyr       | gga att<br>Gly lle<br>60  | ttt gaa<br>Phe Glu        | cga tgt<br>Arg Cys<br>65  | aaa gag<br>Lys Glu        | ttg 307<br>Leu        |          |
| gta gaa gca<br>Val Glu Ala<br>70                  | gga tat g<br>Gly Tyr A        | gat gtc<br>Asp Val<br>75 | agg caa<br>Arg Gln        | cca gat<br>Pro Asp        | aaa gaa<br>Lys Glu<br>80  | aat gtg<br>Asn Val        | tcg 355<br>Ser        |          |
| ctt ctt cat<br>Leu Leu His<br>85                  | tgg gct g<br>Trp Ala A        | Ala lle A                | Asn Asn                   | aga ctg<br>Arg Leu<br>95  | Asp Leu                   | gta aag<br>Val Lys        | ttt 403<br>Phe<br>100 |          |
| tat att tca<br>Tyr IIe Ser                        | aaa ggt g<br>Lys Gly A<br>105 | gct gtt g<br>Na Val N    | gta gat<br>Val Asp        | cag ttg<br>GIn Leu<br>110 | ggt gga<br>Gly Gly        | gat tta<br>Asp Leu<br>115 | aat 451<br>Asn        |          |
| tca act cct<br>Ser Thr Pro                        | ctt cac t<br>Leu His T<br>120 | gg gcc a<br>rp Ala       | atc cga<br>lle Arg<br>125 | caa gga<br>GIn GIy        | cat tta<br>His Leu        | cct atg<br>Pro Met<br>130 | gtc 499<br>Val        |          |
| ata tta tta<br>11e Leu Leu<br>135                 | ctc cag c<br>Leu Gin H        | lis Gly A                | gca gac<br>Ala Asp<br>140 | ccc act<br>Pro Thr        | ctt att<br>Leu lle<br>145 | gat gga<br>Asp Gly        | gag 547<br>Glu        |          |
| gga ttc agc<br>Gly Phe Ser<br>150                 |                               |                          |                           | Leu Phe                   |                           |                           |                       |          |
| ata gca tat                                       | ctc atc t                     | ca aag g                 | gga cag                   | agt gtg                   | aat atg                   | aca gat                   | gta 643               |          |

|            |                   |            |            |                   | _          |            |            |            |                   |            |            |            | _          | _                 |            |      |
|------------|-------------------|------------|------------|-------------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|-------------------|------------|------|
| 11e<br>165 | Ala               | Tyr        | Leu        | He                | 170        | Lys        | Gly        | Gln        | Ser               | Val<br>175 | Asn        | Met        | T          | sp                | Val<br>180 |      |
|            | ggg<br>Gly        |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |            | 691  |
|            | cca<br>Pro        |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |            | 739  |
|            | aaa<br>Lys        |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |            | 787  |
|            | gtt<br>Val<br>230 |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |            | 835  |
|            | cag<br>Gln        |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |            | 883  |
| aaa<br>Lys | aat<br>Asn        | cag<br>Gln | ctc<br>Leu | att<br>Ile<br>265 | att<br>lle | cat<br>His | atg<br>Met | cta<br>Leu | aaa<br>Lys<br>270 | aca<br>Thr | gaa<br>Glu | gcc<br>Ala | aaa<br>Lys | atg<br>Met<br>275 | aga<br>Arg | 931  |
|            | aac<br>Asn        |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |            | 979  |
|            | ctg<br>Leu        |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |            | 1027 |
|            | ttg<br>Leu<br>310 |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |            | 1075 |
|            | aca<br>Thr        |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |            | 1123 |
|            | aag<br>Lys        |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |            | 1171 |
|            | tgg<br>Trp        |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |            | 1219 |
|            | gcc<br>Ala        |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |            | 1267 |
|            | ttt<br>Phe<br>390 |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |            | 1315 |

| tct<br>Ser<br>405 | gaa<br>Glu        | gaa<br>Glu        | gaa<br>Glu        | aag<br>Lys        | aaa<br>Lys<br>410 | gtg<br>Val        | aat<br>Asn        | atc<br>He         | atc<br>Ile        | acc<br>Thr<br>415 | ctt<br>Leu        | gca<br>Ala        | gaa<br>Glu        | act<br>Thr        | ggc<br>Gly<br>420 | 1363   |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|--------|
| tct<br>Ser        | ctg<br>Leu        | gac<br>Asp        | ttc<br>Phe        | aga<br>Arg<br>425 | aca<br>Thr        | ttt<br>Phe        | tgt<br>Cys        | aca<br>Thr        | tca<br>Ser<br>430 | tgt<br>Cys        | ctt<br>Leu        | ata<br>He         | agg<br>Arg        | aag<br>Lys<br>435 | cca<br>Pro        | 1411   |
| tta<br>Leu        | agg<br>Arg        | tca<br>Ser        | ctc<br>Leu<br>440 | cac<br>His        | tgc<br>Cys        | cat<br>His        | gta<br>Val        | tgc<br>Cys<br>445 | aac<br>Asn        | tgc<br>Cys        | tgt<br>Cys        | gtg<br>Val        | gct<br>Ala<br>450 | cga<br>Arg        | tat<br>Tyr        | 1459   |
| gat<br>Asp        | caa<br>G n        | cac<br>His<br>455 | tgc<br>Cys        | ctg<br>Leu        | tgg<br>Trp        | act<br>Thr        | gga<br>Gly<br>460 | cgg<br>Arg        | tgc<br>Cys        | ata<br>Ile        | ggt<br>Gly        | ttt<br>Phe<br>465 | ggc<br>Gly        | aac<br>Asn        | cat<br>His        | 1507   |
| cac<br>His        | tat<br>Tyr<br>470 | tac<br>Tyr        | ata<br>Ile        | ttc<br>Phe        | ttc<br>Phe        | ttg<br>Leu<br>475 | ttt<br>Phe        | ttc<br>Phe        | ctt<br>Leu        | tcc<br>Ser        | atg<br>Met<br>480 | gta<br>Val        | tgt<br>Cys        | ggc<br>Gly        | tgg<br>Trp        | 1555   |
| att<br>lle<br>485 | ata<br>Ile        | tat<br>Tyr        | gga<br>Gly        | tct<br>Ser        | ttc<br>Phe<br>490 | atc<br>Ile        | tat<br>Tyr        | ttg<br>Leu        | tcc<br>Ser        | agt<br>Ser<br>495 | cat<br>His        | tgt<br>Cys        | gcc<br>Ala        | aca<br>Thr        | aca<br>Thr<br>500 | 1603   |
| ttc<br>Phe        | aaa<br>Lys        | gaa<br>Glu        | gat<br>Asp        | gga<br>Gly<br>505 | tta<br>Leu        | tgg<br>Trp        | act<br>Thr        | tac<br>Tyr        | ctc<br>Leu<br>510 | aat<br>Asn        | cag<br>Gln        | att<br>lle        | gtg<br>Val        | gcc<br>Ala<br>515 | tgt<br>Cys        | 1651   |
| tcc<br>Ser        | cct<br>Pro        | tgg<br>Trp        | gtt<br>Vai<br>520 | Leu               | tat<br>Tyr        | atc<br>He         | ttg<br>Leu        | atg<br>Met<br>525 | cta<br>Leu        | gca<br>Ala        | act<br>Thr        | ttc<br>Phe        | cat<br>His<br>530 | ttc<br>Phe        | tca<br>Ser        | 1699 - |
| tgg<br>Trp        | tca<br>Ser        | aca<br>Thr<br>535 | Phe               | tta<br>Leu        | tta<br>Leu        | tta<br>Leu        | aat<br>Asn<br>540 | caa<br>Gln        | ctc<br>Leu        | ttt<br>Phe        | cag<br>Gln        | att<br>  e<br>545 | gcc<br>Ala        | ttt<br>Phe        | ctg<br>Leu        | 1747   |
| ggc<br>Gly        | ctg<br>Leu<br>550 | Thr               | tcc<br>Ser        | cat<br>His        | Glu               | aga<br>Arg<br>555 | He                | Ser               | ctg<br>Leu        | Gln               | Lys               | cag<br>Gln        | agc<br>Ser        | aag<br>Lys        | cat<br>His        | 1795   |
| atg<br>Met<br>565 | Lys               | cag<br>Gln        | acg<br>Thr        | ttg<br>Leu        | tcc<br>Ser<br>570 | Leu               | agg<br>Arg        | aag<br>Lys        | aca<br>Thr        | cca<br>Pro<br>575 | lyr               | aat<br>Asn        | ctt<br>Leu        | gga<br>Gly        | ttc<br>Phe<br>580 | 1843   |
| atg<br>Met        | cag<br>Gln        | aac<br>Asn        | ctg<br>Leu        | gca<br>Ala<br>585 | Asp               | ttc<br>Phe        | ttt<br>Phe        | cag<br>Gin        | tgt<br>Cys<br>590 | Gly               | tgc<br>Cys        | ttt<br>Phe        | ggc<br>Gly        | ttg<br>Leu<br>595 | gtg<br>Val        | 1891   |
| aag<br>Lys        | ccc<br>Pro        | tgt<br>Cys        | gtg<br>Val<br>600 | Val               | gat<br>Asp        | tgg<br>Trp        | aca<br>Thr        | tca<br>Ser<br>605 | Gln               | tac<br>Tyr        | acc<br>Thr        | atg<br>Met        | gto<br>Val<br>610 | Phe               | cac<br>His        | 1939   |
| cca<br>Pro        | gcc<br>Ala        | agg<br>Arg<br>615 | g Gli             | g aag<br>i Lys    | gtt<br>Val        | ctt<br>Leu        | cgc<br>Arg<br>620 | Ser               | gta<br>Val        | tga               | agaa              | naag              | caac              | ccaa              | iaa               | 1989   |
|                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | - 2010 |

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<212> PRT

<213> Homo sapiens

<400> 55

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Asp lle Pro Val Pro Tyr Leu Tyr Phe Asp Met Gly Ala Ala Val Leu 50 55 60

Cys Ala Ser Phe Met Ser Phe Gly Val Lys Arg Arg Trp Phe Ala Leu 65 70 75 80

Gly Ala Ala Leu Gln Leu Ala Ile Ser Thr Tyr Ala Ala Tyr Ile Gly 85 90 95

Gly Tyr Val His Tyr Gly Asp Trp Leu Lys Val Arg Met Tyr Ser Arg 100 105 110

Thr Val Ala IIe IIe Gly Gly Phe Leu Val Leu Ala Ser Gly Ala Gly 115 120 125

Glu Leu Tyr Arg Arg Lys Pro Arg Ser Arg Ser Leu Gln Ser Thr Gly 130 135 140

Gin Val Phe Leu Gly Ile Tyr Leu Ile Cys Val Ala Tyr Ser Leu Gln 145 150 155 160

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Glu Leu Met Ile Gln Leu Phe Phe Val Leu Tyr Gly Ile Leu Ala Leu 180 185 190

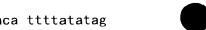
Ala Phe Leu Ser Gly r Tyr Val Thr Leu Ala Ala Gln 195 Val Leu Leu Pro Pro Val Met Leu Leu IIe Asp Gly Asn Val Ala Tyr 210 Trp His Asn Thr Arg Arg Val Glu Phe Trp Asn Gln Met Lys Leu Leu Gly Glu Ser Val Gly lie Phe Gly Thr Ala Val lle Leu Ala Thr Asp 250 Gly <210> 56 <211> 1520 <212> DNA <213> Homo sapiens <220> <221> CDS <222> (10).. (780) <400> 56 tttcccaag atg gcg tcg aag ata ggt tcg aga cgg tgg atg ttg cag ctg 51 Met Ala Ser Lys Ile Gly Ser Arg Arg Trp Met Leu Gln Leu atc atg cag ttg ggt tcg gtg ctg ctc aca cgc tgc ccc ttt tgg ggc 99 lle Met Gln Leu Gly Ser Val Leu Leu Thr Arg Cys Pro Phe Trp Gly 15 tgc ttc agc cag ctc atg ctg tac gct gag agg gct gag gca cgc cgg 147 Cys Phe Ser Gln Leu Met Leu Tyr Ala Glu Arg Ala Glu Ala Arg Arg aag ccc gac atc cca gtg cct tac ctg tat ttc gac atg ggg gca gcc 195 Lys Pro Asp Ile Pro Val Pro Tyr Leu Tyr Phe Asp Met Gly Ala Ala gtg ctg tgc gct agt ttc atg tcc ttt ggc gtg aag cgg cgc tgg ttc 243 Val Leu Cys Ala Ser Phe Met Ser Phe Gly Val Lys Arg Arg Trp Phe 70 gcg ctg ggg gcc gca ctc caa ttg gcc att agc acc tac gcc gcc tac 291 Ala Leu Gly Ala Ala Leu Gln Leu Ala Ile Ser Thr Tyr Ala Ala Tyr 80 85 atc ggg ggc tac gtc cac tac ggg gac tgg ctg aag gtc cgt atg tac 339 lle Gly Gly Tyr Val His Tyr Gly Asp Trp Leu Lys Val Arg Met Tyr 95 tcg cgc aca gtt gcc atc atc ggc ggc ttt ctt gtg ttg gcc agc ggt 387

120

Ser Arg Thr Val Ala lle lle Gly Gly Phe Leu Val Leu Ala Ser Gly

115

| gct ggg gag ctg tad c cgg aaa cct cgc agc cgc tcc cag tcc Ala Gly Glu Leu Tyr Arg Arg Lys Pro Arg Ser Arg Ser Leu Gln Ser 130 135                     |   |
|---|---|
| acc ggc cag gtg ttc ctg ggt atc tac ctc atc tgt gtg gcc tac tca 483 Thr Gly Gln Val Phe Leu Gly Ile Tyr Leu Ile Cys Val Ala Tyr Ser 145 150 155       |   |
| ctg cag cac agc aag gag gac cgg ctg gcg tat ctg aac cat ctc cca Leu Gln His Ser Lys Glu Asp Arg Leu Ala Tyr Leu Asn His Leu Pro 160 165 170           |   |
| gga ggg gag ctg atg atc cag ctg ttc ttc gtg ctg tat ggc atc ctg Gly Gly Glu Leu Met lle Gln Leu Phe Phe Val Leu Tyr Gly lle Leu 175 180 185 190       |   |
| gcc ctg gcc ttt ctg tca ggc tac tac gtg acc ctc gct gcc cag atc Ala Leu Ala Phe Leu Ser Gly Tyr Tyr Val Thr Leu Ala Ala Gln lle 195 200 205           |   |
| ctg gct gta ctg ctg ccc cct gtc atg ctg ctc att gat ggc aat gtt 675<br>Leu Ala Val Leu Leu Pro Pro Val Met Leu Leu Ile Asp Gly Asn Val<br>210 215 220 |   |
| gct tac tgg cac aac acg cgg cgt gtt gag ttc tgg aac cag atg aag Ala Tyr Trp His Asn Thr Arg Arg Val Glu Phe Trp Asn Gln Met Lys 225 230 235           |   |
| ctc ctt gga gag agt gtg ggc atc ttc gga act gct gtc atc ctg gcc 771<br>Leu Leu Gly Glu Ser Val Gly Ile Phe Gly Thr Ala Val Ile Leu Ala<br>240 245 250 |   |
| act gat ggc tgagttttat ggcaagaggc tgagatgggc acagggagcc 820<br>Thr Asp Gly<br>255   |   |
| actgagggtc accetgcett ceteettget ggeccagetg etgtttattt atgetttttg 880   |   |
| gtctgtttgt ttgatctttt gctttttaa aattgtttt tgcagttaag aggcagctca 940   |   |
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<211> 107 <212> PRT

<213> Homo sapiens

<400> 57

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Leu Thr Glu Leu Gln Leu Arg Ala Arg Gln Leu Leu Asp Gln Val Glu 35 40 45

Gln lle Gln Lys Glu Gln Asp Tyr Gln Arg Tyr Arg Glu Glu Arg Phe 50 55 60

Arg Leu Thr Ser Glu Ser Thr Asn Gln Arg Val Leu Trp Trp Ser lle 65 70 75 80

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<400> 58

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Met Ala Leu Phe Ala Gly Gly Lys Leu Arg Val His Leu Asp

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gat aag ctg acg gag cta cag ctc cgc gcc cgc cag ttg ctt gat cag 146 Asp Lys Leu Thr Glu Leu Gin Leu Arg Ala Arg Gin Leu Leu Asp Gin 35 40 45

gtg gaa cag att cag aag gag cag gat tac caa agg tat cgt gaa gag 194 Val Glu Gln lle Gln Lys Glu Gln Asp Tyr Gln Arg Tyr Arg Glu Glu 50 55 60

cgc ttc cga ctg acg agc gag agc acc aac cag agg gtc cta tgg tgg 242

Arg Phe Arg Leu Thr Glu Ser Thr Asn Gln Arg Val Lorp Tr 65 70 75

tcc att gct cag act gtc atc ctc atc ctc act ggc atc tgg cag atg 290 Ser lle Ala Gln Thr Val lle Leu lle Leu Thr Gly lle Trp Gln Met 80 85 90

cgt cac ctc aag agc ttc ttt gag gcc aag aag ctg gtg tagtgccctc 339
Arg His Leu Lys Ser Phe Phe Glu Ala Lys Lys Leu Val
95 100 105

tttgtatgac ccttcctttt tacctcattt atttggtact ttccccacac agtcctttat 399 ccacctggat ttttagggaa aaaaaatgaa aaagaataag tcacattggt tccatggcca 459 caaaccattc agatcagcca cttgctgacc ctggttctta aggacacatg acattagtcc 519 aatctttcaa aatcttgtct tagggcttgt gaggaatcag aactaaccca ggactcagtc 579 ctgcttcttt tgcctcgagt gattttcctc tgtttttcac taaataagca aatgaaaact 639 ctctccatta ccttctgctt tctctttgtc cacttacgca gtaggtgact ggcatgtgcc 699 acagagcagg ccctgcctca ctgtctgctg gtcagttctg ggttcactta atggctttgt 759 gaatgtaaat aaggggcagg tcttggccct agaggattga gatgttttc tatatcttag 819 aactattttt ggataaatta tatattttcc ttcctagtag aagtgttact gcctgtaact 879 agctcaaaat accaatgcag tttctgcatt ctgggttttg ttttctttt tttttttt 939 ttttttgagt tttgctcttg tcgcccaggc tggagtgcaa tggcgtgatc tcagctcact 999 ggcaacatct gcctcccggg ttcaaatgat tctcctgcct cagtctcctg agtagctggg 1059 attacaggtg cccgccacca cgctcagcta atttttgtat ttttagtaga gatggggttt 1119 taccatgttg gccaggctgg tcttagactc ctgacctcag ttgatccacc tgcctcagcc 1179 tctgcattca gtttattcac atatttttgg taactcccat ggcagctcct aggatttcag 1239 cggtctgtgg gccagaaagc aggcaccagg gctgacctca aggccgtatc agagggccaa 1299 gcagagttct tttggatacc tgcttttcat cccacagggc cttagagtca gaggtaaggt 1359 agcaacagag ctagaatggg gcaatgcact cttaccctcc ttctcaactt ttatttaagc 1419 tgtgctaaat gtttcttca agggaaccag atttagttct ttacagaatt ttccagtgaa 1479 ataaaacatg ttgtaat 1496

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<211> 272

<212> PRT

<213> Homo sapiens

<400> 59

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Pro Trp Lys Leu Thr Ala Ser Lys Thr His IIe Met Lys Ser Ala Asp 20 25 30

Val Glu Lys Leu Ala Asp Glu Leu His Met Pro Ser Leu Pro Glu Met 35 40 45

Met Phe Gly Asp Asn Val Leu Arg lle Gln His Gly Ser Gly Phe Gly 50 55 60

lle Glu Phe Asn Ala Thr Asp Ala Leu Arg Cys Val Asn Asn Tyr Gln 65 70 75 80

Gly Met Leu Lys Val Ala Cys Ala Glu Glu Trp Gln Glu Ser Arg Thr 85 90 95

Glu Gly Glu His Ser Lys Glu Val lle Lys Pro Tyr Asp Trp Thr Tyr 100 105 110

Thr Thr Asp Tyr Lys Gly Thr Leu Leu Gly Glu Ser Leu Lys Leu Lys 115 120 125

Val Val Pro Thr Thr Asp His IIe Asp Thr Glu Lys Leu Lys Ala Arg 130 135 140

Glu Gln lle Lys Phe Phe Glu Glu Val Leu Leu Phe Glu Asp Glu Leu 145 150 155 160

His Asp His Gly Val Ser Ser Leu Ser Val Lys Ile Arg Val Met Pro 165 170 175

Ser Ser Phe Phe Leu Leu Leu Arg Phe Phe Leu Arg Ile Asp Gly Val 180 185 190

Leu lle Arg Met Asn Asp Thr Arg Leu Tyr His Glu Ala Asp Lys Thr 195 200 205

Tyr Met Leu Arg Glu Tyr Thr Ser Arg Glu Ser Lys 11e Ser Ser Leu 210 215 220

Met His Val Pro Pro Ser Leu Phe Thr Glu Pro Asn Glu Ile Ser Gln 225 230 235 240

Tyr Leu Pro lle Lys Glu Ala Val Cys Glu Lys Leu lle Phe Pro Glu 245 250 255

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<212> DNA

<213> Homo sapiens

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ago ttt ttc ctg ctg ttg cgg ttt ttc ttg aga att gat ggg gtg ctt Ser Phe Phe Leu Leu Leu Arg Phe Phe Leu Arg I e Asp Gly Val Leu

185

695

| atc aga atg aat gat gag aga ctt tac cat gag gct gac acc tac 74.  Ile Arg Met Asn Asp Thr Arg Leu Tyr His Glu Ala Asp Lys Thr Tyr  195 200 205            | 3  |
|--|----|
| atg tta cga gaa tat acg tca cga gaa agc aaa att tct agt ttg atg 79<br>Met Leu Arg Glu Tyr Thr Ser Arg Glu Ser Lys ile Ser Ser Leu Met<br>210 215 220 225 | 1  |
| cat gtt cca cct tcc ctc ttc acg gaa cct aat gaa ata tcc cag tat 839<br>His Val Pro Pro Ser Leu Phe Thr Glu Pro Asn Glu Ile Ser Gln Tyr<br>230 235 240    | 9  |
| tta cca ata aag gaa gca gtt tgt gag aag cta ata ttt cca gaa aga 887<br>Leu Pro Ile Lys Glu Ala Val Cys Glu Lys Leu Ile Phe Pro Glu Arg<br>245 250 255    | 7  |
| att gat cct aac cca gca gac tca caa aaa agt aca caa gtg gaa 932<br>lie Asp Pro Asn Pro Ala Asp Ser Gin Lys Ser Thr Gin Val Giu<br>260 265 270            | 2  |
| taaaatgtga tacaacatat actcactatg gaatctgact ggacaccttg gctatttgta 992  | 2  |
| aggggttatt tttattatga gaattaattg ccttgtttat gtacagattt tctgtagcct 105  | 52 |
| taaaggaaaa aaaaataaag atcgttacag gcaggtttca ctcaactgct atttgtactg 111  | 2  |
| tctgtcttca cattcatatt ccagatttat attttctgga gttaaatttg gatgatttct 117  | 12 |
| aaattatcac aaagtgggac ctcagcagta gtgatgtgtg tgtctcatga gcagtgagca 123  | 32 |
| cagtctgcat tcatcatgaa acactatctt ctaccaggag gaggttaatg taaatcacca 129  | 2  |
| aatcccaatg ccttgtgact ttcataggat tcctgatcat gcatgttgat gtactggctc 135  | 2  |
| ttcactttgg gctttctgat gtttattcac acctttggag agttgcaact tgccacatac 141  | 2  |
| gaaattagtc tcatagtgta gtgaacttca accccaaaat tttaaaaaatg tatttccccc 147   | 2  |
| cagttttaaa ttgcctttga aatttaaaaa aaaaaattta gacttagtac cagaaccaaa 153  | 2  |
| aatacctaga tttttggaga acttattaca tacatagaaa catgaatatg gtttaccwct 159  | 2  |
| gtgtgtgtgt gtgtgtgt gtgtatacag acttttttt ttaacttgtt gattcagatg 165   | 2  |
| tcttggtccc tgaatagtcc tagattactt attttgagaa ttgattgtta aaaattacag 1712   | 2  |
| ggaattaaaa taattgcctt tttttttta gagggtaaga gatgggtaga agagtatgcc 1772  | 2  |
| tctgaaaatt ttattagttt attcttgtgg agaataccaa gaaaatgtgt atttgcccat 1832   | 2  |
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Leu Thr Asp Cys Ile Gly Thr Val Asp Ser Arg Ala Glu Ser Ile Asp

Lys Lys Ile Ser Arg Leu Asp Ala Glu Leu Val Lys Tyr Lys Asp Gln

lie Lys Lys Met Arg Glu Gly Pro Ala Lys Asn Met Val Lys Gln Lys

Ala Leu Arg Val Leu Lys Gln Lys Arg Met Tyr Glu Gln Gln Arg Asp

Asn Leu Ala Gin Gin Ser Phe Asn Met Glu Gin Ala Asn Tyr Thr lle

Gin Ser Leu Lys Asp Thr Lys Thr Thr Val Asp Ala Met Lys Leu Gly 105

Val Lys Glu Met Lys Lys Ala Tyr Lys Gln Val Lys Ile Asp Gln Ile

Glu Asp Leu Gln Asp Gln Leu Glu Asp Met Met Glu Asp Ala Asn Glu 130

lle Gln Glu Ala Leu Ser Arg Ser Tyr Gly Thr Pro Glu Leu Asp Glu 150 155

Asp Asp Leu Glu Ala Glu Leu Asp Ala Leu Gly Asp Glu Leu Leu Ala

Asp Glu Asp Ser Ser Tyr Leu Asp Glu Ala Ala Ser Ala Pro Ala Ile 185 180

Pro Glu Gly Val Pro Thr Asp Thr Lys Asn Lys Asp Gly Val Leu Val 200 205

Asp Glu Phe Gly Leu Pro Gln Ile Pro Ala Ser 210 215

<210> 62

<211> 1362

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (49).. (705)

<400> 62

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|                    |                   |                   |                   | •                 |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |     |
|--------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-----|
| ctc<br>Leu         | ttc<br>Phe<br>5   | ggg<br>Gly        | aaa<br>Lys        | gcg<br>Ala        | aaa<br>Lys        | ccc<br>Pro<br>10  | aag<br>Lys        | gct<br>Ala        | ccg<br>Pro        | ccg<br>Pro        | ccc<br>Pro<br>15  | agc<br>Ser        | ctg<br>Leu        | act<br>Thr        | gac<br>Asp        | 105 |
| tgc<br>Cys<br>20   | att<br>Ile        | ggc<br>Gly        | acg<br>Thr        | gtg<br>Val        | gac<br>Asp<br>25  | agt<br>Ser        | aga<br>Arg        | gca<br>Ala        | gaa<br>Glu        | tcc<br>Ser<br>30  | att<br>lle        | gac<br>Asp        | aag<br>Lys        | aag<br>Lys        | att<br>Ile<br>35  | 153 |
| tct<br>Ser         | cga<br>Arg        | ttg<br>Leu        | gat<br>Asp        | gct<br>Ala<br>40  | gag<br>Glu        | cta<br>Leu        | gtg<br>Val        | aag<br>Lys        | tat<br>Tyr<br>45  | aag<br>Lys        | gat<br>Asp        | cag<br>Gln        | atc<br>lle        | aag<br>Lys<br>50  | aag<br>Lys        | 201 |
| atg<br>Met         | aga<br>Arg        | gag<br>Glu        | ggt<br>Gly<br>55  | cct<br>Pro        | gca<br>Ala        | aag<br>Lys        | aat<br>Asn        | atg<br>Met<br>60  | gtc<br>Val        | aag<br>Lys        | cag<br>Gln        | aaa<br>Lys        | gcc<br>Ala<br>65  | ttg<br>Leu        | cga<br>Arg        | 249 |
| gtt<br>Val         | tta<br>Leu        | aag<br>Lys<br>70  | caa<br>G n        | aag<br>Lys        | agg<br>Arg        | atg<br>Met        | tat<br>Tyr<br>75  | gag<br>Glu        | cag<br>Gln        | cag<br>Gln        | cgg<br>Arg        | gac<br>Asp<br>80  | aat<br>Asn        | ctt<br>Leu        | gcc<br>Ala        | 297 |
| caa<br>Gln         | cag<br>Gln<br>85  | tca<br>Ser        | ttc<br>Phe        | aac<br>Asn        | atg<br>Met        | gaa<br>Glu<br>90  | caa<br>Gln        | gcc<br>Ala        | aat<br>Asn        | tat<br>Tyr        | acc<br>Thr<br>95  | atc<br>Ile        | cag<br>Gln        | tct<br>Ser        | ttg<br>Leu        | 345 |
| aag<br>Lys<br>100  | gac<br>Asp        | acc<br>Thr        | aag<br>Lys        | acc<br>Thr        | acg<br>Thr<br>105 | gtt<br>Val        | gat<br>Asp        | gct<br>Ala        | atg<br>Met        | aaa<br>Lys<br>110 | ctg<br>Leu        | gga<br>Gly        | gta<br>Val        | aag<br>Lys        | gaa<br>Glu<br>115 | 393 |
| atg<br>Met         | aag<br>Lys        | aag<br>Lys        | gca<br>Ala        | tac<br>Tyr<br>120 | aag<br>Lys        | caa<br>Gln        | gtg<br>Val        | aag<br>Lys        | atc<br>lle<br>125 | gac<br>Asp        | cag<br>Gln        | att<br>He         | gag<br>Glu        | gat<br>Asp<br>130 | tta<br>Leu        | 441 |
| caa<br>Gln         | gac<br>Asp        | cag<br>Gln        | cta<br>Leu<br>135 | gag<br>Glu        | gat<br>Asp        | atg<br>Met        | atg<br>Met        | gaa<br>Glu<br>140 | gat<br>Asp        | gca<br>Ala        | aat<br>Asn        | gaa<br>Glu        | atc<br>Ile<br>145 | caa<br>Gln        | gaa<br>Glu        | 489 |
| gca<br>Ala         | ctg<br>Leu        | agt<br>Ser<br>150 | cgc<br>Arg        | agt<br>Ser        | tat<br>Tyr        | ggc<br>Gly        | acc<br>Thr<br>155 | cca<br>Pro        | gaa<br>Glu        | ctg<br>Leu        | gat<br>Asp        | gaa<br>Glu<br>160 | gat<br>Asp        | gat<br>Asp        | tta<br>Leu        | 537 |
| g <b>aa</b><br>Glu | gca<br>Ala<br>165 | gag<br>Glu        | ttg<br>Leu        | gat<br>Asp        | gca<br>Ala        | cta<br>Leu<br>170 | ggt<br>Gly        | gat<br>Asp        | gag<br>Glu        | ctt<br>Leu        | ctg<br>Leu<br>175 | gct<br>Ala        | gat<br>Asp        | gaa<br>Glu        | gac<br>Asp        | 585 |
| agt<br>Ser<br>180  | tct<br>Ser        | tat<br>Tyr        | ttg<br>Leu        | gat<br>Asp        | gag<br>Glu<br>185 | gca<br>Ala        | gca<br>Ala        | tct<br>Ser        | gca<br>Ala        | cct<br>Pro<br>190 | gca<br>Ala        | att<br>Ile        | cca<br>Pro        | gaa<br>Glu        | ggt<br>Gly<br>195 | 633 |
| gtt<br>Val         | ccc<br>Pro        | act<br>Thr        | gat<br>Asp        | aca<br>Thr<br>200 | aaa<br>Lys        | aac<br>Asn        | aag<br>Lys        | gat<br>Asp        | gga<br>Gly<br>205 | gtt<br>Val        | ctg<br>Leu        | gtg<br>Val        | gat<br>Asp        | gaa<br>Glu<br>210 | ttt<br>Phe        | 681 |
| gga<br>Gly         | ttg<br>Leu        | cca<br>Pro        | cag<br>Gln<br>215 | atc<br>Ile        | cct<br>Pro        | gct<br>Ala        | tca<br>Ser        | tag               | attt              | gca               | tcat              | tcaa              | gc a              | tatc <sup>,</sup> | ttgta             | 735 |

ttaggtttct ttcctttctt tgaaggaaag tttaattaca ttgctcttt atttttcca 855
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tggaattatc actactgtat catgagtggg tattttgatt ctatggtcc ctcagtatta 1275
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<211> 622

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<213> Homo sapiens

<400> 63

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Leu Leu His Pro Glu Glu IIe Lys Pro Gln Ser His Tyr Asn His Gly
20 25 30

Tyr Gly Glu Pro Leu Gly Arg Lys Thr His IIe Asp Asp Tyr Ser Thr 35 40 45

Trp Asp Ile Val Lys Ala Thr Gln Tyr Gly Ile Tyr Glu Arg Cys Arg 50 55 60

Glu Leu Val Glu Ala Gly Tyr Asp Val Arg Gln Pro Asp Lys Glu Asn 65 70 75 80

Val Thr Leu Leu His Trp Ala Ala IIe Asn Asn Arg IIe Asp Leu Val 85 90 95

Lys Tyr Tyr lle Ser Lys Gly Ala lle Val Asp Gln Leu Gly Gly Asp 100 105 110

Leu Asn Ser Thr Pro Leu His Trp Ala Thr Arg Gln Gly His Leu Ser 115 120 125

Met Val Val Gin Leu Met Lys Tyr Gly Ala Asp Pro Ser Leu Ile Asp 130 135 140

Gly Glu Gly Cys Ser Cys Ile His Leu Ala Ala Gln Phe Gly His Thr 145 150 155 160

| Ser        | He         | Val        | Ala        | 165        | Leu        | ılle        | Ala        | Lys        | Gly<br>170 |            | Asp        | Val        | Asp        | Met<br>175 |            |
|------------|------------|------------|------------|------------|------------|-------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| Asp        | Gln        | Asn        | Gly<br>180 |            | Thr        | Pro         | Leu        | Met<br>185 |            | Ala        | Ala        | Tyr        | Arg<br>190 |            | His        |
| Ser        | Val        | Asp<br>195 |            | Thr        | Arg        | Leu         | Leu<br>200 |            | . Thr      | Phe        | Asn        | Val<br>205 |            | Val        | Asr        |
| Leu        | Gly<br>210 |            | Lys        | Tyr        | His        | Lys<br>215  |            | Thr        | Ala        | l Leu      | His<br>220 |            | Ala        | Val        | Leu        |
| Ala<br>225 | Gly        | Asn        | Thr        | Thr        | Val<br>230 |             | Ser        | Leu        | Leu        | Leu<br>235 |            | Ala        | Gly        | Ala        | Asn<br>240 |
| Val        | Asp        | Ala        | Gln        | Asn<br>245 | lle        | Lys         | Gly        | Glu        | Ser<br>250 |            | Leu        | Asp        | Leu        | Ala<br>255 | -          |
| Gin        | Arg        | Lys        | Asn<br>260 |            | Trp        | Met         | lle        | Asn<br>265 |            | Leu        | Gln        | Glu        | Ala<br>270 | _          | Gln        |
| Ala        | Lys        | Gly<br>275 | Tyr        | Asp        | Asn        | Pro         | Ser<br>280 | Phe        | Leu        | Arg        | Lys        | Leu<br>285 | Lys        | Ala        | Asp        |
| Lys        | Glu<br>290 | Phe        | Arg        | Gln        | Lys        | Va l<br>295 | Met        | Leu        | Gly        | Thr        | Pro<br>300 | Phe        | Leu        | Val        | lle        |
| Trp<br>305 | Leu        | Val        | Gly        | Phe        | lle<br>310 | Ala         | Asp        | Leu        | Asn        | 11e<br>315 | Asp        | Ser        | Trp        | Leu        | lle<br>320 |
| Lys        | Gly        | Leu        | Met-       | Tyr<br>325 | Gly        | Gly         | Val        | Trp        | Ala<br>330 | Thr        | Vai        | Gln        | Phe        | Leu<br>335 | Ser        |
| Lys        | Ser        | Phe        | Phe<br>340 | Asp        | His        | Ser         | Met        | His<br>345 | Ser        | Ala        | Leu        | Pro        | Leu<br>350 | Gly        | He         |
| Tyr        | Leu        | Ala<br>355 | Thr        | Lys        | Phe        | Trp         | Met<br>360 | Tyr        | Val        | Thr        | Trp        | Phe<br>365 | Phe        | Trp        | Phe        |
| Trp        | Asn<br>370 | Asp        | Leu        | Asn        | Phe        | Leu<br>375  | Phe        | lle        | His        | Leu        | Pro<br>380 | Phe        | Leu        | Ala        | Asn        |
| Ser<br>385 | Val        | Ala        | Leu        | Phe        | Tyr<br>390 | Asn         | Phe        | G∣y        | Lys        | Ser<br>395 | Trp        | Lys        | Ser        | Asp        | Pro<br>400 |
| Gly        | lle        | lle        | Lys        | Ala<br>405 | Thr        | Glu         | Glu        | Gln        | Lys<br>410 | Lys        | Lys        | Thr        | lle        | Val<br>415 | Glu        |
| Leu        | Ala        | Glu        | Thr<br>420 | Gly        | Ser        | Leu         | Asp        | Leu<br>425 | Ser        | He         | Phe        | Cys        | Ser<br>430 | Thr        | Cys        |
| _eu        |            | Arg<br>435 | Lys        | Pro        | Val        | Arg         | Ser<br>440 | Lys        | His        | Cys        | Gly        | Val<br>445 | Cys        | Asn        | Arg        |
|            | lle<br>450 | Ala        | Lys        | Phe        | Asp        | His<br>455  | His        | Cys        | Pro        | Trp        | Val<br>460 | Gly        | Asn        | Cys        | Val        |

| Gly<br>465       | Ala                              | a Gly            | / Asr      | n Hid          | 470              |                  | Phe              | Met          | Gly            | Tyr<br>475       |                  | Phe              | ·             | Leu            | Leu<br>480       |      |
|------------------|----------------------------------|------------------|------------|----------------|------------------|------------------|------------------|--------------|----------------|------------------|------------------|------------------|---------------|----------------|------------------|------|
| Phe              | Met                              | . He             | : Cys      | Trp<br>485     | Met              | : lle            | Tyr              | Gly          | Cys<br>490     |                  | Ser              | Tyr              | Trp           | Gly<br>495     | Leu              |      |
| His              | Cys                              | Glu              | Thr<br>500 | Thr            | Tyr              | Thr              | Lys              | Asp<br>505   | Gly            | Phe              | Trp              | Thr              | Tyr<br>510    |                | Thr              |      |
| Gln              | He                               | Ala<br>515       | Thr        | Cys            | Ser              | Pro              | Trp<br>520       |              | Phe            | Trp              | Met              | Phe<br>525       |               | Asn            | Ser              |      |
| Val              | Phe<br>530                       | His              | Phe        | Met            | Trp              | Val<br>535       | Ala              | Val          | Leu            | Leu              | Met<br>540       | Cys              | Gln           | Met            | Tyr              |      |
| GIn<br>545       | lle                              | Ser              | Cys        | Leu            | Gly<br>550       | lle              | Thr              | Thr          | Asn            | G1u<br>555       | Arg              | Met              | Asn           | Ala            | Arg<br>560       |      |
| Arg              | Tyr                              | Lys              | His        | Phe<br>565     | Lys              | Val              | Thr              | Thr          | Thr<br>570     | Ser              | He               | Glu              | Ser           | Pro<br>575     | Phe              |      |
| Asn              | His                              | Gly              | Cys<br>580 | Val            | Arg              | Asn              | He               | 11e<br>585   | Asp            | Phe              | Phe              | Glu              | Phe<br>590    | Arg            | Cys              |      |
| Cys              | Gly                              | Leu<br>595       | Phe        | Arg            | Pro              | Val              | lle<br>600       | Val          | Asp            | Trp              | Thr              | Arg<br>605       | Gln           | Tyr            | Thr              |      |
| lle              | Glu<br>610                       | Tyr              | Asp        | Gln            | lle              | Ser<br>615       | Gly              | Ser          | Gly            | Tyr              | Gln<br>620       | Leu              | Val           |                |                  |      |
| <211<br><212     | 0> 64<br> > 29<br> > DN<br> > Ho | 948<br>NA        | sapie      | ens            |                  |                  |                  |              |                |                  |                  |                  |               |                |                  |      |
|                  | > CC                             |                  | (187       | 79)            |                  |                  |                  |              |                |                  |                  |                  |               |                |                  |      |
|                  | > 64<br>aaca                     |                  | nag a<br>M | ntg g<br>Met A | cg g<br>la A     | gac g<br>Nsp G   | gc c             | cg g<br>ro A | gat g<br>Nsp G | ag t<br>Ilu T    | ac g<br>yr A     | at a<br>sp T     | icc g<br>hr 0 | gaa g<br>Glu A | cg<br>la         | 49   |
| ggc<br>Gly       | tgt<br>Cys                       | gtg<br>Val<br>15 | ccc<br>Pro | ctt<br>Leu     | ctc<br>Leu       | cac<br>His       | cca<br>Pro<br>20 | gag<br>Glu   | gaa<br>Glu     | atc<br>lle       | aaa<br>Lys       | ccc<br>Pro<br>25 | caa<br>Gln    | agc<br>Ser     | cat<br>His       | 97   |
| tat<br>Tyr       | aac<br>Asn<br>30                 | cat<br>His       | gga<br>Gly | tat<br>Tyr     | ggt<br>G!y       | gaa<br>Glu<br>35 | cct<br>Pro       | ctt<br>Leu   | gga<br>Gly     | cgg<br>Arg       | aaa<br>Lys<br>40 | act<br>Thr       | cat<br>His    | att<br>He      | gat<br>Asp       | 145  |
| gat<br>Asp<br>45 | tac<br>Tyr                       | agc<br>Ser       | aca<br>Thr | tgg<br>Trp     | gac<br>Asp<br>50 | ata<br>Ile       | gtc<br>Val       | aag<br>Lys   | gct<br>Ala     | aca<br>Thr<br>55 | caa<br>Gln       | tat<br>Tyr       | gga<br>Gly    | ata<br>He      | tat<br>Tyr<br>60 | 193  |
| gaa (            | cgc                              | tet              | сда        | gaa            | ttø              | øtø.             | gaa              | σca          | oot ·          | tat i            | at.              | nt a             | caa           | caa            | 000              | 2/11 |

| Glu | Arg | Cys | Arg | Glu<br>65 |                   | Val | Glu | Ala | Gly<br>70 | Tyr | Asp | Val | A | l n<br>75 | Pro |     |
|-----|-----|-----|-----|-----------|-------------------|-----|-----|-----|-----------|-----|-----|-----|---|-----------|-----|-----|
|     |     |     |     |           | acc<br>Thr        |     |     |     |           |     |     |     |   |           |     | 289 |
|     |     |     |     |           | tac<br>Tyr        |     |     |     |           |     |     |     |   |           |     | 337 |
|     |     |     |     |           | aat<br>Asn        |     |     |     |           |     |     |     |   |           |     | 385 |
|     |     |     |     |           | gtt<br>Val<br>130 |     |     |     |           |     |     |     |   |           |     | 433 |
|     |     |     |     |           | gaa<br>Glu        |     |     |     |           |     |     |     |   |           |     | 481 |
|     |     |     |     |           | att<br>lle        |     |     |     |           |     |     |     |   |           |     | 529 |
|     |     |     |     |           | cag<br>Gln        |     |     |     |           |     |     |     |   |           |     | 577 |
|     |     |     |     |           | gtg<br>Val        |     |     |     |           |     |     |     |   |           |     | 625 |
|     |     |     |     |           | ggt<br>Gly<br>210 |     |     |     |           |     |     |     |   |           |     | 673 |
|     |     |     |     |           | ggg<br>Gly        |     |     |     |           |     |     |     |   |           |     | 721 |
|     |     |     |     |           | gat<br>Asp        |     |     |     |           |     |     |     |   |           |     | 769 |
|     |     |     |     |           | aga<br>Arg        |     |     |     |           |     |     |     |   |           |     | 817 |
|     |     |     |     |           | aaa<br>Lys        |     |     |     |           |     |     |     |   |           |     | 865 |
|     |     |     |     |           | gaa<br>Glu<br>290 |     |     |     |           |     |     |     |   |           |     | 913 |

|                   |                   |            |            |                   |                   |                   |            |            |                   |                   |                   |            | 1          |                   |                   |      |
|-------------------|-------------------|------------|------------|-------------------|-------------------|-------------------|------------|------------|-------------------|-------------------|-------------------|------------|------------|-------------------|-------------------|------|
| ttc<br>Phe        | cta<br>Leu        | gtt<br>Val | att<br>He  | tgg<br>Trp<br>305 | ctg<br>Leu        | gtt<br>Val        | ggg<br>G y | ttt<br>Phe | ata<br>  e<br>310 | gca<br>Ala        | gac<br>Asp        | cta<br>Leu | aat<br>Asn | att<br>lle<br>315 | gat<br>Asp        | 961  |
|                   | tgg<br>Trp        |            |            | Lys               |                   |                   |            |            |                   |                   |                   |            |            |                   |                   | 1009 |
|                   | ttt<br>Phe        |            | Ser        |                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   | 1057 |
| ccc<br>Pro        | ctt<br>Leu<br>350 | ggg<br>Gly | ata<br>Ile | tat<br>Tyr        | ttg<br>Leu        | gca<br>Ala<br>355 | acc<br>Thr | aaa<br>Lys | ttc<br>Phe        | tgg<br>Trp        | atg<br>Met<br>360 | tat<br>Tyr | gtg<br>Val | acg<br>Thr        | tgg<br>Trp        | 1105 |
| ttc<br>Phe<br>365 | ttc<br>Phe        | tgg<br>Trp | ttt<br>Phe | tgg<br>Trp        | aat<br>Asn<br>370 | gat<br>Asp        | ctc<br>Leu | aac<br>Asn | ttt<br>Phe        | tta<br>Leu<br>375 | ttt<br>Phe        | atc<br>lle | cat<br>His | ctt<br>Leu        | cca<br>Pro<br>380 | 1153 |
|                   | ctt<br>Leu        |            |            |                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   | 1201 |
|                   | tca<br>Ser        |            |            |                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   | 1249 |
|                   | ata<br>Ile        |            |            |                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   | 1297 |
|                   | agt<br>Ser<br>430 |            |            |                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   | 1345 |
|                   | tgc<br>Cys        |            |            | Cys               |                   |                   |            |            |                   |                   |                   |            |            |                   | gtg<br>Val<br>460 | 1393 |
|                   | aac<br>Asn        |            |            |                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   | 1441 |
|                   | ttc<br>Phe        |            |            |                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   | 1489 |
|                   | tgg<br>Trp        |            |            |                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   | 1537 |
|                   | tac<br>Tyr<br>510 |            |            |                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   | 1585 |
| ttc               | ctg               | aac        | agt        | gtt               | ttc               | cac               | ttc        | atg        | tgg               | gtg               | gct               | gta        | tta        | ctc               | atg               | 1633 |

| Phe Leu<br>525            | Asn               | Ser               |                   | e<br>530          | His               | Phe               | Met               | Trp               | Val<br>535        |                   | Val               |                   | Leu               | Met<br>540        |      |
|---------------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| tgt cag<br>Cys Gln        | atg<br>Met        | lyr               | cag<br>Gln<br>545 | ata<br>He         | tca<br>Ser        | tgt<br>Cys        | tta<br>Leu        | ggt<br>Gly<br>550 | att<br>Ile        | act<br>Thr        | aca<br>Thr        | aat<br>Asn        | gaa<br>Glu<br>555 | aga<br>Arg        | 1681 |
| atg aat<br>Met Asn        | Ala.              | agg<br>Arg<br>560 | aga<br>Arg        | tac<br>Tyr        | aag<br>Lys        | cac<br>His        | ttt<br>Phe<br>565 | aaa<br>Lys        | gtc<br>Val        | aca<br>Thr        | aca<br>Thr        | acg<br>Thr<br>570 | tct<br>Ser        | att<br>  e        | 1729 |
| gaa agc<br>Glu Ser        | cca<br>Pro<br>575 | ttc<br>Phe        | aac<br>Asn l      | cat<br>His        | gga<br>Gly        | tgt<br>Cys<br>580 | gta<br>Val        | aga<br>Arg        | aat<br>Asn        | att<br>He         | ata<br>  e<br>585 | gac<br>Asp        | ttc<br>Phe        | ttt<br>Phe        | 1777 |
| gaa ttt<br>Glu Phe<br>590 | cga<br>Arg (      | tgc<br>Cys (      | tgt (<br>Cys (    | ggc<br>Gly        | ctc<br>Leu<br>595 | ttt<br>Phe        | cgt<br>Arg        | cct<br>Pro        | gtt<br>Val        | atc<br>lle<br>600 | gtg<br>Val        | gac<br>Asp        | tgg<br>Trp        | acc<br>Thr        | 1825 |
| agg cag<br>Arg Gln<br>605 | tat a<br>Tyr i    | aca a<br>Thr      | lle (             | gaa<br>Glu<br>610 | tat<br>Tyr        | gac<br>Asp        | caa<br>Gln        | ata<br>Ile        | tca<br>Ser<br>615 | gga<br>Gly        | tct<br>Ser        | ggg<br>Gly        | tac<br>Tyr        | cag<br>Gln<br>620 | 1873 |
| ctg gtg<br>Leu Val        | tagce             | gacat             | tc tt             | atc               | ctat              | g aa              | gcat              | attg              | ctg               | gagtg             | gtg               | cctg              | gaaaa             | tt                | 1929 |
| gtgtctgt                  | cc gt             | tgtct             | tttct             | са                | cact              | cgaa              | tcc               | acat              | cct               | ttga              | acaa              | ga g              | catg              | ctatg             | 1989 |
| tgtagggc                  | ta at             | ggtg              | gaatt             | : tt              | acag              | tctt              | ttt               | ttca              | aca               | cttt              | tatt              | aa c              | aaaa              | gtaaa             | 2049 |
| catggaca                  | ga ac             | acac              | etgcc             | at                | ttct              | ggga              | aga               | gtaa              | aga               | tgat              | aaaa              | aa t              | aatt              | ttaat             | 2109 |
| ggttctta                  | at gt             | ggaa              | atto              | ac                | aaca <sup>.</sup> | tact              | caa               | cttt              | tgg               | gttt              | tgtt              | ct c              | acag              | tattt             | 2169 |
| ttcacaaa                  | aa aa             | gggt              | aaac              | tta               | attc              | tatt              | gac               | agac              | atg               | gtgt              | actga             | at c              | agaa              | atgtt             | 2229 |
| cagtttta                  | ac ta             | aaac              | taaa              | tt                | tatg              | ttat              | ttg               | gcta              | aat               | gtta              | tgatį             | gc a              | gtct              | agtac             | 2289 |
| gagtattg                  | ca tc             | taat              | tcca              | gga               | agcat             | ttgt              | ttta              | aagt              | tga ·             | ttga              | ctag              | tt a              | ttat              | gtaca             | 2349 |
| tttcagaa                  | tg ta             | caca              | taaa              | tad               | ctgtg             | gatg              | aaaa              | atcat             | tgt į             | gatt              | gggat             | tc t              | actg              | tgatg             | 2409 |
| ttgtcttc                  | aa ag             | gcag              | gaga              | aaa               | ataat             | gtt               | caca              | aataa             | aaa <sup>-</sup>  | tgtgo             | ctaad             | ca a              | tgtt              | ttgtt             | 2469 |
| tctatcag                  | ct gt             | tgca              | atgc              | tga               | atata             | attt              | ctag              | gttca             | agt į             | gaaat             | taatt             | tt g              | tagt              | aacct             | 2529 |
| tactctga                  | gg tt             | ttac              | ggtc              | tga               | ataat             | gaa               | gcac              | ettgo             | cat @             | gagta             | atagt             | a a               | gtca              | tgttt             | 2589 |
| ttttgttc                  | aa at             | ttaa              | aagc              | cct               | gcta              | att               | gcat              | gaca              | aca o             | ccaca             | ataga             | a t               | gtata             | actag             | 2649 |
| cagatacta                 | at cca            | agtg              | aagc              | ata               | aatt              | aga               | attt              | aatt              | tg a              | atgtt             | caaa              | a a               | cagti             | ccat              | 2709 |
| ttttaaggg                 | gt taa            | aggt              | ggta              | ttt               | tcaa              | gaa               | aagg              | caga              | ac a              | aata              | atgo              | a aa              | aatto             | tcag              | 2769 |
| taatagtga                 | at aca            | atgga             | atat              | act               | tcct              | ttt               | aaat              | tctc              | ag c              | etgca             | aaat              | a at              | ttgta             | igaca             | 2829 |
| aaataatgg                 | gc att            | ttaad             | ctaa              | aga               | tgga              | gca               | tgat              | ctgt              | gt a              | cata              | gcac              | a tg              | gtgaa             | itaaa             | 2889 |

<210> 65

<211> 632

<212> PRT

<213> Homo sapiens

<400> 65

Met Gln Arg Glu Glu Gly Phe Asn Thr Lys Met Ala Asp Gly Pro Asp

Glu Tyr Asp Thr Glu Ala Gly Cys Val Pro Leu Leu His Pro Glu Glu

lle Lys Pro Gln Ser His Tyr Asn His Gly Tyr Gly Glu Pro Leu Gly

Arg Lys Thr His Ile Asp Asp Tyr Ser Thr Trp Asp Ile Val Lys Ala

Thr Gin Tyr Gly lle Tyr Glu Arg Cys Arg Glu Leu Val Glu Ala Gly

Tyr Asp Val Arg Gln Pro Asp Lys Glu Asn Val Thr Leu Leu His Trp

Ala Ala ile Asn Asn Arg ile Asp Leu Vai Lys Tyr Tyr ile Ser Lys

Gly Ala lle Val Asp Gln Leu Gly Gly Asp Leu Asn Ser Thr Pro Leu

His Trp Ala Thr Arg Gln Gly His Leu Ser Met Val Val Gln Leu Met

Lys Tyr Gly Ala Asp Pro Ser Leu lle Asp Gly Glu Gly Cys Ser Cys 145

lle His Leu Ala Ala Gln Phe Gly His Thr Ser Ile Val Ala Tyr Leu

lle Ala Lys Gly Gln Asp Val Asp Met Met Asp Gln Asn Gly Met Thr

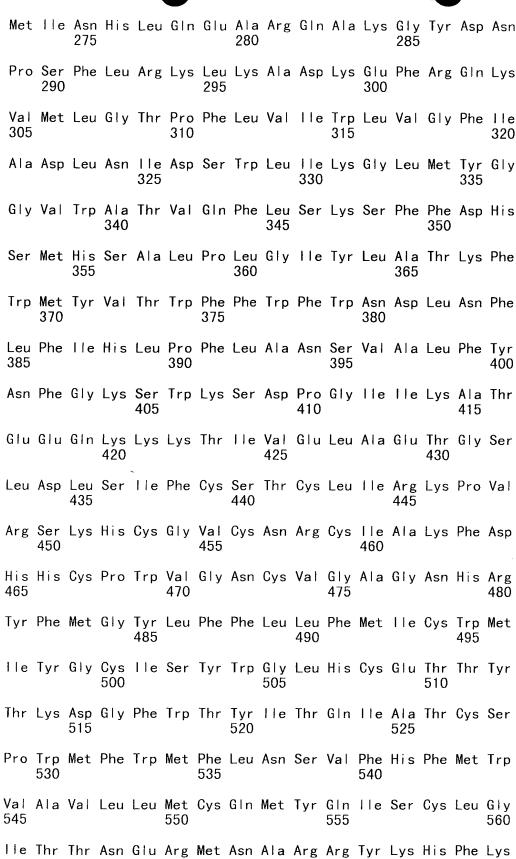
Pro Leu Met Trp Ala Ala Tyr Arg Thr His Ser Val Asp Pro Thr Arg

Leu Leu Leu Thr Phe Asn Val Ser Val Asn Leu Gly Asp Lys Tyr His

Lys Asn Thr Ala Leu His Trp Ala Val Leu Ala Gly Asn Thr Thr Val 225 230 240

lle Ser Leu Leu Glu Ala Gly Ala Asn Val Asp Ala Gln Asn lle 245 250

Lys Gly Glu Ser Ala Leu Asp Leu Ala Lys Gln Arg Lys Asn Val Trp



| Val Thr Thr   | Thr Ser<br>580     | lle Glu                  | Ser        | Pro<br>585 | Phe        | Asn        | His              | Gly        | Cys<br>590 | Val        | Arg        |     |
|---|--------------------|--------------------------|------------|------------|------------|------------|------------------|------------|------------|------------|------------|-----|
| Asn lle lle<br>595                                  | Asp Phe            | Phe Glu                  | Phe<br>600 | Arg        | Cys        | Cys        | Gly              | Leu<br>605 | Phe        | Arg        | Pro        |     |
| Val IIe Val<br>610                                  | Asp Trp            | Thr Arg<br>615           |            | Tyr        | Thr        | lle        | Glu<br>620       | Tyr        | Asp        | Gln        | lle        |     |
| Ser Gly Ser<br>625                                  | Gly Tyr            | Gin Leu<br>630           | Val        |            |            |            |                  |            |            |            |            |     |
| <210> 66<br><211> 4715<br><212> DNA<br><213> Homo s | sapiens            |                          |            |            |            |            |                  |            |            |            |            |     |
| <220><br><221> CDS<br><222> (108).                  | . (2003)           |                          |            |            |            |            |                  |            |            |            |            |     |
| <400> 66<br>gaagaaggag g                            | gaggaggco          | cc gcgtc                 | gccto      | c cgg      | gcggg      | ggct       | cgc              | gctc       | gcc (      | ccgce      | gctcgc     | 60  |
| cctccgcctc g  | gcccgagco          | cc cggga                 | gggtg      | g aaa      | acgct      | ttc        | tcc              | cagc       |            | cag<br>Gln |            | 116 |
| gag gag gga<br>Glu Glu Gly<br>5                     | ttt aac<br>Phe Asn | acc aag<br>Thr Lys<br>10 | Met        | gcg<br>Ala | gac<br>Asp | ggc<br>G y | ccg<br>Pro<br>15 | gat<br>Asp | gag<br>Glu | tac<br>Tyr | gat<br>Asp | 164 |
| acc gaa gcg<br>Thr Glu Ala<br>20                    |                    |                          |            |            |            |            |                  |            |            |            |            | 212 |
| caa agc cat<br>GIn Ser His                          |                    |                          |            |            |            |            |                  |            |            |            |            | 260 |
| cat att gat<br>His Ile Asp                          |                    |                          |            |            |            |            |                  |            |            |            |            | 308 |
| gga ata tat<br>Gly lle Tyr<br>70                    |                    |                          |            |            |            |            |                  |            |            |            |            | 356 |
| cgg caa ccg<br>Arg Gln Pro<br>85                    |                    |                          |            |            |            |            |                  |            |            |            |            | 404 |
| aat aac aga<br>Asn Asn Arg<br>100                   |                    |                          |            |            |            |            |                  |            |            |            |            | 452 |

| gtg<br>Val        | gat<br>Asp        | caa<br>G\n        | ctt<br>Leu        | gg.<br>G y<br>120 | g<br>Gly          | gac<br>Asp        | ctg<br>Leu        | aat<br>Asn        | tca<br>Ser<br>125 | act<br>Thr        | cca<br>Pro        | ttg<br>Leu        | His               | tgg<br>Trp<br>130 | gcc<br>Ala                     | 500  |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|--------------------------------|------|
| aca<br>Thr        | aga<br>Arg        | caa<br>Gln        | ggc<br>Gly<br>135 | cat<br>His        | cta<br>Leu        | tcc<br>Ser        | atg<br>Met        | gtt<br>Val<br>140 | gtg<br>Val        | caa<br>Gln        | cta<br>Leu        | atg<br>Met        | aaa<br>Lys<br>145 | tat<br>Tyr        | ggt<br>Gly                     | 548  |
| gca<br>Ala        | gat<br>Asp        | cct<br>Pro<br>150 | tca<br>Ser        | tta<br>Leu        | att<br>Ile        | gat<br>Asp        | gga<br>Gly<br>155 | gaa<br>Glu        | gga<br>Gly        | tgt<br>Cys        | agc<br>Ser        | tgt<br>Cys<br>160 | att<br>lle        | cat<br>His        | ctg<br>Leu                     | 596  |
| gct<br>Ala        | gct<br>Ala<br>165 | cag<br>G n        | ttc<br>Phe        | gga<br>Gly        | cat<br>His        | acc<br>Thr<br>170 | tca<br>Ser        | att<br>He         | gtt<br>Val        | gct<br>Ala        | tat<br>Tyr<br>175 | ctc<br>Leu        | ata<br>He         | gca<br>Ala        | aaa<br>Lys                     | 644  |
| gga<br>Gly<br>180 | cag<br>Gln        | gat<br>Asp        | gta<br>Val        | gat<br>Asp        | atg<br>Met<br>185 | atg<br>Met        | gat<br>Asp        | cag<br>Gln        | aat<br>Asn        | gga<br>Gly<br>190 | atg<br>Met        | acg<br>Thr        | cct<br>Pro        | tta<br>Leu        | atg<br>Met<br>195              | 692  |
| tgg<br>Trp        | gca<br>Ala        | gca<br>Ala        | tat<br>Tyr        | aga<br>Arg<br>200 | aca<br>Thr        | cat<br>His        | agt<br>Ser        | gtg<br>Val        | gat<br>Asp<br>205 | cca<br>Pro        | act<br>Thr        | aga<br>Arg        | ttg<br>Leu        | ctt<br>Leu<br>210 | tta<br>Leu                     | 740  |
| aca<br>Thr        | ttc<br>Phe        | aat<br>Asn        | gtt<br>Val<br>215 | tca<br>Ser        | gtt<br>Val        | aac<br>Asn        | ctt<br>Leu        | ggt<br>Gly<br>220 | gac<br>Asp        | aag<br>Lys        | tat<br>Tyr        | cac<br>His        | aaa<br>Lys<br>225 | aac<br>Asn        | act<br>Thr                     | 788  |
| gct<br>Ala        | ctg<br>Leu        | cat<br>His<br>230 | tgg<br>Trp        | gca<br>Ala        | gtg<br>Val        | cta<br>Leu        | gca<br>Ala<br>235 | ggg<br>Gly        | aat<br>Asn        | acc<br>Thr        | aca<br>Thr        | gtc<br>Val<br>240 | att<br>He         | agc<br>Ser        | ctt<br>Leu                     | 836  |
| ctt<br>Leu        | ctg<br>Leu<br>245 | gaa<br>Glu        | gct<br>Ala        | gga<br>Gly        | gct<br>Ala        | aat<br>Asn<br>250 | gtt<br>Val        | gat<br>Asp        | gcc<br>Ala        | cag<br>Gln        | aat<br>Asn<br>255 | atc<br>lle        | aag<br>Lys        | ggc<br>Gly        | gaa<br>Glu                     | 884  |
| tca<br>Ser<br>260 | gcg<br>Ala        | ctt<br>Leu        | gat<br>Asp        | ttg<br>Leu        | gca<br>Ala<br>265 | aaa<br>Lys        | cag<br>Gln        | aga<br>Arg        | Lys               | aat<br>Asn<br>270 | gtg<br>Val        | tgg<br>Trp        | atg<br>Met        | atc<br>He         | aac<br>Asn <sup>*</sup><br>275 | 932  |
| cac<br>His        | tta<br>Leu        | caa<br>Gln        | gag<br>Glu        | gca<br>Ala<br>280 | agg<br>Arg        | caa<br>G n        | gca<br>Ala        | aaa<br>Lys        | gga<br>Gly<br>285 | tat<br>Tyr        | gac<br>Asp        | aat<br>Asn        | ccg<br>Pro        | tcc<br>Ser<br>290 | ttc<br>Phe                     | 980  |
| ctt<br>Leu        | aga<br>Arg        | aag<br>Lys        | ctg<br>Leu<br>295 | aaa<br>Lys        | gct<br>Ala        | gat<br>Asp        | aag<br>Lys        | gaa<br>Glu<br>300 | ttt<br>Phe        | cgg<br>Arg        | cag<br>G n        | aaa<br>Lys        | gta<br>Val<br>305 | atg<br>Met        | tta<br>Leu                     | 1028 |
| gga<br>Gly        | act<br>Thr        | cct<br>Pro<br>310 | ttc<br>Phe        | cta<br>Leu        | gtt<br>Val        | att<br>He         | tgg<br>Trp<br>315 | ctg<br>Leu        | gtt<br>Val        | ggg<br>Gly        | ttt<br>Phe        | ata<br>11e<br>320 | gca<br>Ala        | gac<br>Asp        | cta<br>Leu                     | 1076 |
| aat<br>Asn        | att<br>Ile<br>325 | gat<br>Asp        | tct<br>Ser        | tgg<br>Trp        | ctc<br>Leu        | att<br>  e<br>330 | aaa<br>Lys        | ggg<br>Gly        | cta<br>Leu        | atg<br>Met        | tat<br>Tyr<br>335 | ggt<br>Gly        | ggt<br>Gly        | gtt<br>Val        | tgg<br>Trp                     | 1124 |
| gct<br>Ala        | aca<br>Thr        | gta<br>Val        | cag<br>Gln        | ttt<br>Phe        | ctt<br>Leu        | tca<br>Ser        | aaa<br>Lys        | tcc<br>Ser        | ttt<br>Phe        | ttc<br>Phe        | gat<br>Asp        | cat<br>His        | tca<br>Ser        | atg<br>Met        | cat<br>His                     | 1172 |

| agt<br>Ser        | gca<br>Ala        | ttg<br>Leu        | ccc<br>Pro        | ctt<br>Leu<br>360 | ggg<br>Gly        | ata<br>Ile        | tat<br>Tyr        | ttg<br>Leu        | gca<br>Ala<br>365 | acc<br>Thr        | aaa<br>Lys        | ttc<br>Phe         | tgg<br>Trp        | atg<br>Met<br>370 | tat<br>Tyr        | 1220 |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|--------------------|-------------------|-------------------|-------------------|------|
| gtg<br>Val        | acg<br>Thr        | tgg<br>Trp        | ttc<br>Phe<br>375 | ttc<br>Phe        | tgg<br>Trp        | ttt<br>Phe        | tgg<br>Trp        | aat<br>Asn<br>380 | gat<br>Asp        | ctc<br>Leu        | aac<br>Asn        | ttt<br>Phe         | tta<br>Leu<br>385 | ttt<br>Phe        | atc<br>ile        | 1268 |
| cat<br>His        | ctt<br>Leu        | cca<br>Pro<br>390 | ttc<br>Phe        | ctt<br>Leu        | gcc<br>Ala        | aat<br>Asn        | agt<br>Ser<br>395 | gtt<br>Val        | gca<br>Ala        | ctt<br>Leu        | ttc<br>Phe        | tac<br>Tyr<br>400  | aat<br>Asn        | ttt<br>Phe        | gga<br>Gly        | 1316 |
| aaa<br>Lys        | tct<br>Ser<br>405 | tgg<br>Trp        | aaa<br>Lys        | tca<br>Ser        | gat<br>Asp        | cca<br>Pro<br>410 | ggg<br>Gly        | att<br>lle        | att<br>lle        | aaa<br>Lys        | gca<br>Ala<br>415 | aca<br>Thr         | gaa<br>Glu        | gag<br>Glu        | caa<br>Gln        | 1364 |
| aag<br>Lys<br>420 | aaa<br>Lys        | aag<br>Lys        | aca<br>Thr        | ata<br>Ile        | gtt<br>Val<br>425 | gaa<br>Glu        | ctt<br>Leu        | gca<br>Ala        | gag<br>Glu        | aca<br>Thr<br>430 | gga<br>Gly        | agt<br>Ser         | ctg<br>Leu        | gac<br>Asp        | ctc<br>Leu<br>435 | 1412 |
| agt<br>Ser        | ata<br>  e        | ttc<br>Phe        | tgc<br>Cys        | agt<br>Ser<br>440 | acc<br>Thr        | tgt<br>Cys        | ttg<br>Leu        | ata<br>Ile        | cga<br>Arg<br>445 | aaa<br>Lys        | ccg<br>Pro        | gtg<br>Val         | agg<br>Arg        | tcc<br>Ser<br>450 | aaa<br>Lys        | 1460 |
| cat<br>His        | tgt<br>Cys        | ggt<br>Gly        | gtg<br>Val<br>455 | Cys               | aac<br>Asn        | cgc<br>Arg        | tgt<br>Cys        | ata<br>11e<br>460 | gca<br>Ala        | aaa<br>Lys        | ttt<br>Phe        | gat<br>Asp         | cat<br>His<br>465 | cat<br>His        | tgc<br>Cys        | 1508 |
| cca<br>Pro        | tgg<br>Trp        | gtg<br>Val<br>470 | Gly               | alac<br>Asn       | tgt<br>Cys        | gta<br>Val        | ggt<br>Gly<br>475 | gca<br>Ala        | ggc<br>Gly        | aac<br>Asn        | cat<br>His        | aga<br>Arg<br>480  | tat<br>Tyr        | ttt<br>Phe        | atg<br>Met        | 1556 |
| ggc<br>Gly        | tac<br>Tyr<br>485 | Leu               | ttc<br>Phe        | ttc<br>Phe        | ttg<br>Leu        | ctt<br>Leu<br>490 | ttt<br>Phe        | atg<br>Met        | atc<br>lle        | tgc<br>Cys        | tgg<br>Trp<br>495 | atg<br>Met         | att<br>He         | tat<br>Tyr        | ggt<br>Gly        | 1604 |
| tgt<br>Cys<br>500 | Пe                | tct<br>Ser        | tac<br>Tyr        | tgg<br>Trp        | gga<br>Gly<br>505 | Leu               | His               | Cys               | Glu               | Ihr               | Ihr               | tac<br>Tyr         | Inr               | Lys               | ASP               | 1652 |
| gga<br>Gly        | ttt<br>Phe        | tgg<br>Trp        | aca<br>Thr        | tac<br>Tyr<br>520 | lle               | act<br>Thr        | cag<br>Gln        | att<br>lle        | gcc<br>Ala<br>525 | lhr               | tgt<br>Cys        | tca<br>Ser         | cct<br>Pro        | tgg<br>Trp<br>530 | atg<br>Met        | 1700 |
| ttt<br>Phe        | tgg<br>Trp        | atg<br>Met        | tto<br>Phe<br>535 | : Leu             | aac<br>Asn        | agt<br>Ser        | gtt<br>Val        | tto<br>Phe<br>540 | His               | ttc<br>Phe        | atg<br>Met        | g tgg<br>Trp       | gtg<br>Val<br>545 | Ala               | gta<br>Val        | 1748 |
| tta<br>Leu        | cto<br>Leu        | atg<br>Met<br>550 | Cys               | cag<br>Glr        | g atg<br>Met      | tac<br>Tyr        | cag<br>Gln<br>555 | lle               | tca<br>Ser        | tgt<br>Cys        | tta<br>Lei        | aggt<br>Gly<br>560 | ' IIE             | act<br>Thr        | aca<br>Thr        | 1796 |
| aat<br>Asr        | gaa<br>Glu<br>565 | ı Arg             | atg<br>Met        | g aat<br>: Asr    | gcc<br>Ala        | agg<br>Arg<br>570 | ; Arg             | tac<br>Tyr        | aag<br>Lys        | g cac<br>s His    | ttt<br>Phe<br>575 | e Lys              | gto<br>Val        | aca<br>Thr        | aca<br>Thr        | 1844 |

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Pro Leu Glu Lys Asn Gly lle lle Thr Gly Tyr Gln lle Ser Trp Glu 340 345 350

Val Tyr Gly Arg Asn Asp Ser Arg Leu Thr His Thr Leu Asn Ser Thr 355 360 365

Met His Glu Tyr Lys Ile Gln Gly Leu Ser Ser Leu Thr Thr Tyr Thr 370 380

lle Asp Val Ala Ala Val Thr Ala Val Gly Thr Gly Leu Val Thr Ser 385 390 395 400

Ser Thr lle Ser Ser Gly Val Pro Pro Asp Leu Pro Gly Ala Pro Ser 405 410 415

Asn Leu Val IIe Ser Asn IIe Ser Pro Arg Ser Ala Thr Leu Gln Phe 420 425 430

Arg Pro Gly Tyr Asp Gly Lys Thr Ser lle Ser Arg Trp lle Val Glu 435 440 445

Gly Gln Met Arg Pro Glu Gly Val Gly Leu Pro Ala Glu Val Thr Gln 450 455 460

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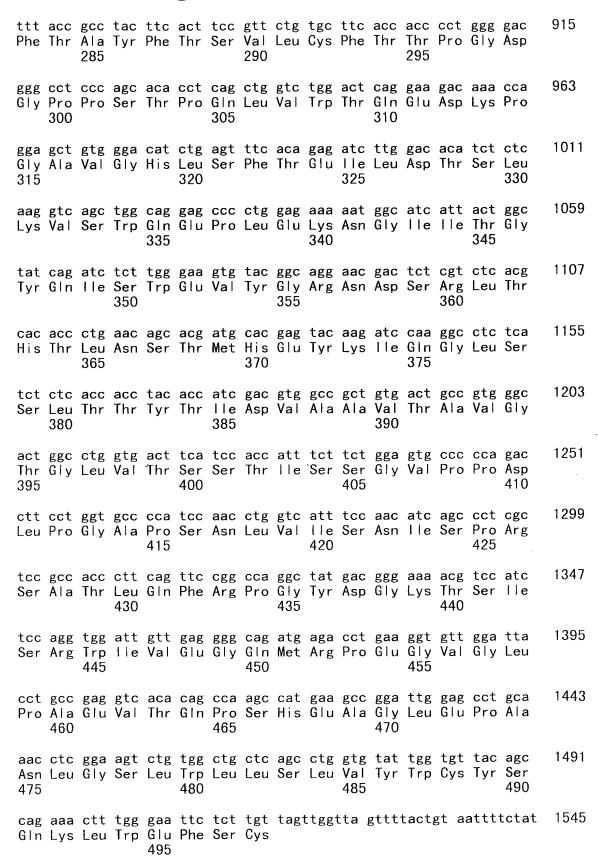
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Ser His 20 25

gcc gtg gtg ctc tct tgg gtc cgg ccc ttt gat gga aac agt cct att 147 Ala Val Val Leu Ser Trp Val Arg Pro Phe Asp Gly Asn Ser Pro lle 30 35 40

| ctt<br>Leu        | tat<br>Tyr        | tac<br>Tyr<br>45  | atc<br>He         | gtg<br>Val        | g<br>G l u        | ctg<br>Leu        | tct<br>Ser<br>50  | gaa<br>Glu        | aac<br>Asn        | aac<br>Asn        | tct<br>Ser                | cca<br>Pro<br>55  | t.<br>Trp         | aag<br>Lys        | gtg<br>Val        | 195 |
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| cat<br>His        | ctg<br>Leu<br>60  | tca<br>Ser        | aac<br>Asn        | gtt<br>Val        | ggc<br>Gly        | cct<br>Pro<br>65  | gag<br>Glu        | atg<br>Met        | aca<br>Thr        | ggc<br>Gly        | gtc<br>Val<br>70          | acc<br>Thr        | gtg<br>Val        | agt<br>Ser        | ggc<br>Gly        | 243 |
| ctg<br>Leu<br>75  | act<br>Thr        | ccg<br>Pro        | gct<br>Ala        | cgt<br>Arg        | acc<br>Thr<br>80  | tat<br>Tyr        | caa<br>Gln        | ttc<br>Phe        | cgg<br>Arg        | gtg<br>Val<br>85  | tgc<br>Cys                | gcg<br>Ala        | gtg<br>Val        | aat<br>Asn        | gaa<br>Glu<br>90  | 291 |
| gtg<br>Val        | ggc<br>Gly        | agg<br>Arg        | ggc<br>Gly        | cag<br>Gln<br>95  | tac<br>Tyr        | agt<br>Ser        | gcc<br>Ala        | gag<br>Glu        | aca<br>Thr<br>100 | agc<br>Ser        | agg<br>Arg                | ttg<br>Leu        | atg<br>Met        | cta<br>Leu<br>105 | cct<br>Pro        | 339 |
| gaa<br>Glu        | gaa<br>Glu        | cca<br>Pro        | ccc<br>Pro<br>110 | agt<br>Ser        | gct<br>Ala        | ccc<br>Pro        | ccg<br>Pro        | aaa<br>Lys<br>115 | aat<br>Asn        | ata<br>Ile        | gtg<br>Val                | gcc<br>Ala        | agt<br>Ser<br>120 | ggg<br>Gly        | cgg<br>Arg        | 387 |
| act<br>Thr        | aat<br>Asn        | cag<br>Gln<br>125 | tcc<br>Ser        | att<br>lle        | atg<br>Met        | gtc<br>Val        | cag<br>Gin<br>130 | tgg<br>Trp        | cag<br>Gln        | cca<br>Pro        | ccc<br>Pro                | cca<br>Pro<br>135 | gaa<br>Glu        | aca<br>Thr        | gag<br>Glu        | 435 |
| cac<br>His        | aac<br>Asn<br>140 | ggg<br>Gly        | gtg<br>Val        | ttg<br>Leu        | cgt<br>Arg        | gga<br>Gly<br>145 | tac<br>Tyr        | atc<br>Ile        | ctc<br>Leu        | agg<br>Arg        | tac<br>Tyr<br>15 <u>0</u> | cgc<br>Arg        | ctg<br>Leu        | gct<br>Ala        | ggc<br>Gly        | 483 |
| ctt<br>Leu<br>155 | ccc<br>Pro        | gga<br>Gly        | gag<br>Glu        | tac<br>Tyr        | cag<br>Gln<br>160 | cag<br>G n        | cgg<br>Arg        | aac<br>Asn        | atc<br>Ile        | acc<br>Thr<br>165 | Ser                       | ccg<br>Pro        | gag<br>Glu        | gtg<br>Val        | aac<br>Asn<br>170 | 531 |
| tac<br>Tyr        | tgc<br>Cys        | ctg<br>Leu        | gtg<br>Val        | aca<br>Thr<br>175 | gac<br>Asp        | ctg<br>Leu        | atc<br>Ile        | atc<br>Ile        | tgg<br>Trp<br>180 | aca<br>Thr        | cag<br>Gln                | tat<br>Tyr        | gag<br>G u        | ata<br>Ile<br>185 | cag<br>Gln        | 579 |
| gtg<br>Val        | gcg<br>Ala        | gcg<br>Ala        | tac<br>Tyr<br>190 | aac<br>Asn        | ggg<br>Gly        | gcc<br>Ala        | ggt<br>Gly        | ctg<br>Leu<br>195 | ggc<br>Gly        | gtc<br>Val        | ttc<br>Phe                | agc<br>Ser        | agg<br>Arg<br>200 | АТА               | gtg<br>Val        | 627 |
| acc<br>Thr        | gag<br>Glu        | tac<br>Tyr<br>205 | acc<br>Thr        | ttg<br>Leu        | cag<br>G n        | gga<br>Gly        | gtg<br>Val<br>210 | Pro               | acc<br>Thr        | gcg<br>Ala        | ccc<br>Pro                | ccg<br>Pro<br>215 | cag<br>Gln        | aac<br>Asn        | gtg<br>Val        | 675 |
| cag<br>Gln        | acg<br>Thr<br>220 | Glu               | gcc<br>Ala        | gtg<br>Val        | aac<br>Asn        | tcc<br>Ser<br>225 | Thr               | acc<br>Thr        | att<br>lle        | cag<br>Gln        | tto<br>Phe<br>230         | Leu               | tgg<br>Trp        | aac<br>Asn        | cct<br>Pro        | 723 |
| ccg<br>Pro<br>235 | Pro               | cag<br>G n        | cag<br>G¦n        | ttt<br>Phe        | atc<br>ile<br>240 | Asn               | ggc<br>Gly        | atc<br>lle        | aac<br>Asn        | cag<br>Gln<br>245 | ıGly                      | tac<br>Tyr        | aag<br>Lys        | ctt<br>Leu        | ctg<br>Leu<br>250 | 771 |
| gca<br>Ala        | tgg<br>Trp        | ccg<br>Pro        | gca<br>Ala        | gat<br>Asp<br>255 | Ala               | ccc<br>Pro        | gag<br>Glu        | gct<br>Ala        | gtc<br>Val<br>260 | Ihr               | gtg<br>Val                | g gtc<br>Val      | act<br>Thr        | att<br>11e<br>265 | gcc<br>Ala        | 819 |
| cca<br>Pro        | gat<br>Asp        | tto<br>Phe        | cac<br>His        | gga<br>Gly        | gtc<br>Val        | cac<br>His        | cat<br>His        | gga<br>Gly        | cac<br>His        | ata<br>He         | a acg<br>e Thr            | g aac<br>Asr      | ctg<br>Leu        | g aag<br>Lys      | g aag<br>S Lys    | 867 |



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Leu Ser Glu Asn Asn Ser Pro Trp Lys Val His Leu Ser Asn Val Gly 50 60

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Pro Pro Lys Asn Ile Val Ala Ser Gly Arg Thr Asn Gln Ser Ile Met 115 120 125

Val Gln Trp Gln Pro Pro Pro Glu Thr Glu His Asn Gly Val Leu Arg 130 135 140

Gly Tyr lle Leu Arg Tyr Arg Leu Ala Gly Leu Pro Gly Glu Tyr Gln 145 150 155 160

Gln Arg Asn Ile Thr Ser Pro Glu Val Asn Tyr Cys Leu Val Thr Asp 165 170 175

Leu Ile Ile Trp Thr Gln Tyr Glu Ile Gln Val Ala Ala Tyr Asn Gly 180 185 190

Ala Gly Leu Gly Val Phe Ser Arg Ala Val Thr Glu Tyr Thr Leu Gln 195 200 205

o Pro Gin Asn Val Gin Thr Glu 🚾 Val Asn Gly Val Pro Thr All 215 Ser Thr Thr lle Gln Phe Leu Trp Asn Pro Pro Pro Gln Gln Phe lle 230 Asn Gly lle Asn Gln Gly Tyr Lys Leu Leu Ala Trp Pro Ala Asp Ala 245 Pro Glu Ala Val Thr Val Val Thr Ile Ala Pro Asp Phe His Gly Val 265 His His Gly His Ile Thr Asn Leu Lys Lys Phe Thr Ala Tyr Phe Thr Ser Val Leu Cys Phe Thr Thr Pro Gly Asp Gly Pro Pro Ser Thr Pro 295 Gln Leu Val Trp Thr Gln Glu Asp Lys Pro Gly Ala Val Gly His Leu 315 310 Ser Phe Thr Glu lie Leu Asp Thr Ser Leu Lys Val Ser Trp Gln Glu Pro Leu Glu Lys Asn Gly lle lle Thr Gly Tyr Gln lle Ser Trp Glu 345 Val Tyr Gly Arg Asn Asp Ser Arg Leu Thr His Thr Leu Asn Ser Thr 365 360 Thr His Glu Tyr Lys Ile Gln Gly Leu Ser Ser Leu Thr Thr Tyr Thr 375 lle Asp Val Ala Ala Val Thr Ala Val Gly Thr Gly Leu Val Thr Ser 400 395 Ser Thr lie Ser Ser Gly Val Pro Pro Asp Leu Pro Gly Ala Pro Ser Asn Leu Val Ile Ser Asn Ile Ser Pro Arg Ser Ala Thr Leu Gin Phe 425 Arg Pro Gly Tyr Asp Gly Lys Thr Ser Ile Ser Arg Trp Ile Val Glu 435 Gly Gln Met Arg His Gln Gly Val Gly Leu Pro Ala Glu Val Thr Gln 455 Pro Ser His Glu Ala Gly Leu Glu Pro Ala Asn Leu Gly Ser Leu Trp 480 475 Leu Leu Ser Leu Val Tyr Trp Cys Tyr Ser Gln Lys Leu Trp Glu Phe 490 485

Ser Cys

| <210> 70<br><211> 1902<br><212> DNA<br><213> Homo sapiens   |     |
|---|-----|
| <220> <221> CDS <222> (22) (1515)   |     |
| <pre>&lt;400&gt; 70 gaaggaggga atgactccag g atg gcc cgg ctg gaa gtg att gaa ctg cct 5</pre>   | 1   |
| cat toa cot cag aac oto otg gto ago cot aat tot too cac ago cac 9 His Ser Pro Gln Asn Leu Leu Val Ser Pro Asn Ser Ser His Ser His 15 20 25            | 9   |
| gcc gtg gtg ctc tct tgg gtc cgg ccc ttt gat gga aac agt cct att 1 Ala Val Val Leu Ser Trp Val Arg Pro Phe Asp Gly Asn Ser Pro Ile 30 35 40            | 47  |
| ctt tat tac atc gtg gag ctg tct gaa aac aac tct cca tgg aag gtg 1<br>Leu Tyr Tyr lle Val Glu Leu Ser Glu Asn Asn Ser Pro Trp Lys Val<br>45 50 55      | 95  |
| cat ctg tca aac gtt ggc cci gag atg aca ggc gtc acc gtg agt ggc 2<br>His Leu Ser Asn Val Gly Pro Glu Met Thr Gly Val Thr Val Ser Gly<br>60 65 70      | 243 |
| ctg act ccg gct cgt acc tat caa ttc cgg gtg tgc gcg gtg aat gaa 2<br>Leu Thr Pro Ala-Arg Thr Tyr Gin Phe Arg Val Cys Ala Val Asn Giu<br>75 80 85 90   | 291 |
| gtg ggc agg ggc cag tac agt gcc gag aca agc agg ttg atg cta cct Val Gly Arg Gly Gin Tyr Ser Ala Glu Thr Ser Arg Leu Met Leu Pro 95 100 105            | 339 |
| gaa gaa cca ccc agt gct ccc ccg aaa aat ata gtg gcc agt ggg cgg Glu Glu Pro Pro Ser Ala Pro Pro Lys Asn Ile Val Ala Ser Gly Arg 110 115 120           | 387 |
| act aat cag too att atg gto cag tgg cag coa coo coa gaa aca gag Thr Asn Gln Ser lie Met Val Gln Trp Gln Pro Pro Pro Glu Thr Glu 125 130 135           | 435 |
| cac aac ggg gtg ttg cgt gga tac atc ctc agg tac cgc ctg gct ggc His Asn Gly Val Leu Arg Gly Tyr lle Leu Arg Tyr Arg Leu Ala Gly 140 145 150           | 483 |
| ctt ccc gga gag tac cag cag cgg aac atc acc agc ccg gag gtg aac<br>Leu Pro Gly Glu Tyr Gln Gln Arg Asn lle Thr Ser Pro Glu Val Asn<br>155 160 165 170 | 531 |
| tac tgc ctg gtg aca gac ctg atc atc tgg aca cag tat gag ata cag Tyr Cys Leu Val Thr Asp Leu IIe IIe Trp Thr GIn Tyr Glu IIe GIn 175 180 185           | 579 |

| gtg<br>Val        | gcg<br>Ala        | gcg<br>Ala        | tac<br>Tyr<br>190 | aac<br>Asn        | g<br>Gly          | gcc<br>Ala        | ggt<br>Gly        | ctg<br>Leu<br>195 | ggc<br>Gly        | gtc<br>Val        | ttc<br>Phe        | agc<br>Ser        | ag<br>Arg<br>200  | gca<br>Ala        | gtg<br>Val          | 627  |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|---------------------|------|
| acc<br>Thr        | gag<br>Glu        | tac<br>Tyr<br>205 | acc<br>Thr        | ttg<br>Leu        | cag<br>Gin        | gga<br>Gly        | gtg<br>Val<br>210 | ccc<br>Pro        | acc<br>Thr        | gcg<br>Ala        | ccc<br>Pro        | ccg<br>Pro<br>215 | cag<br>Gln        | aac<br>Asn        | gtg<br>Val          | 675  |
| cag<br>Gln        | acg<br>Thr<br>220 | gaa<br>Glu        | gcc<br>Ala        | gtg<br>Val        | aac<br>Asn        | tcc<br>Ser<br>225 | acc<br>Thr        | acc<br>Thr        | att<br>lle        | cag<br>Gln        | ttc<br>Phe<br>230 | ctg<br>Leu        | tgg<br>Trp        | aac<br>Asn        | cct<br>Pro          | 723  |
| ccg<br>Pro<br>235 | cct<br>Pro        | cag<br>Gln        | cag<br>Gln        | ttt<br>Phe        | atc<br>Ile<br>240 | aat<br>Asn        | ggc<br>Gly        | atc<br>lle        | aac<br>Asn        | cag<br>Gln<br>245 | gga<br>Gly        | tac<br>Tyr        | aag<br>Lys        | ctt<br>Leu        | ctg<br>Leu<br>250   | 771  |
| gca<br>Ala        | tgg<br>Trp        | ccg<br>Pro        | gca<br>Ala        | gat<br>Asp<br>255 | gcc<br>Ala        | ccc<br>Pro        | gag<br>Glu        | gct<br>Ala        | gtc<br>Val<br>260 | act<br>Thr        | gtg<br>Val        | gtc<br>Val        | act<br>Thr        | att<br>Ile<br>265 | gcc<br>Ala          | 819  |
| cca<br>Pro        | gat<br>Asp        | ttc<br>Phe        | cac<br>His<br>270 | gga<br>Gly        | gtc<br>Val        | cac<br>His        | cat<br>His        | gga<br>Gly<br>275 | cac<br>His        | ata<br>  e        | acg<br>Thr        | aac<br>Asn        | ctg<br>Leu<br>280 | aag<br>Lys        | aag<br>Lys          | 867  |
| ttt<br>Phe        | acc<br>Thr        | gcc<br>Ala<br>285 | tac<br>Tyr        | ttc<br>Phe        | act<br>Thr        | tcc<br>Ser        | gtt<br>Val<br>290 | ctg<br>Leu        | tgc<br>Cys        | ttc<br>Phe        | acc<br>Thr        | acc<br>Thr<br>295 | cct<br>Pro        | ggg<br>Gly        | gac<br>Asp          | 915  |
| ggg<br>Gly        | cct<br>Pro<br>300 | Pro               | agc<br>Ser        | aca<br>Thr        | cct<br>Pro        | cag<br>Gln<br>305 | ctg<br>Leu        | gtc<br>Val        | tgg<br>Trp        | act<br>Thr        | cag<br>Gln<br>310 | gaa<br>Glu        | gac<br>Asp        | aaa<br>Lys        | cca<br>Pro          | 963  |
| gga<br>Gly<br>315 | gct<br>Ala        | gtg<br>Val        | gga<br>G¦y        | cat<br>His        | ctg<br>Leu<br>320 | agt<br>Ser        | ttc<br>Phe        | aca<br>Thr        | gag<br>Glu        | atc<br>Ile<br>325 | ttg<br>Leu        | gac<br>Asp        | aca<br>Thr        | tct<br>Ser        | ctc<br>Leu<br>330   | 1011 |
| aag<br>Lys        | gtc<br>Val        | agc<br>Ser        | tgg<br>Trp        | cag<br>Gln<br>335 | gag<br>Glu        | ccc<br>Pro        | ctg<br>Leu        | gag<br>Glu        | aaa<br>Lys<br>340 | aat<br>Asn        | ggc<br>Gly        | atc<br>  e        | att<br>Ile        | act<br>Thr<br>345 | ggc<br>Gly          | 1059 |
| tat<br>Tyr        | cag<br>Gln        | atc<br>lle        | tct<br>Ser<br>350 | Trp               | gaa<br>Glu        | gtg<br>Val        | tac<br>Tyr        | ggc<br>Gly<br>355 | Arg               | aac<br>Asn        | gac<br>Asp        | tct<br>Ser        | cgt<br>Arg<br>360 | Leu               | acg<br>Thr          | 1107 |
| cac<br>His        | acc<br>Thr        | ctg<br>Leu<br>365 | Asn               | agc<br>Ser        | acg<br>Thr        | acg<br>Thr        | cac<br>His<br>370 | Glu               | tac<br>Tyr        | aag<br>Lys        | ; atc             | Gln<br>375        | Gly               | ctc<br>Leu        | tca<br>Ser          | 1155 |
| tct<br>Ser        | ctc<br>Leu<br>380 | Thr               | acc<br>Thr        | tac<br>Tyr        | acc<br>Thr        | atc<br>11e<br>385 | Asp               | gtg<br>Val        | gcc               | gct<br>Ala        | gtg<br>Val<br>390 | lhr               | gcc               | gtg<br>Val        | g ggc<br>Gly        | 1203 |
| act<br>Thr<br>395 | Gly               | ctg<br>Leu        | gtg<br>Val        | act<br>Thr        | tca<br>Ser<br>400 | Ser               | acc<br>Thr        | att<br>lle        | tct<br>Ser        | tet<br>Ser<br>405 | Gly               | gtg<br>Val        | ccc<br>Pro        | cca<br>Pro        | a gac<br>Asp<br>410 | 1251 |
| ctt<br>Leu        | cct<br>Pro        | ggt<br>Gly        | gcc               | cca<br>Pro        | tcc<br>Ser        | aac<br>Asr        | ctg<br>Leu        | g gto<br>u Val    | att<br>lle        | tcc<br>Ser        | aac<br>Asr        | ato<br>Ile        | ago<br>Ser        | cct<br>Pro        | cgc<br>Arg          | 1299 |



|                   |            |                   |                   | 710        |                   |            |                   |                   | 120        |                   |            |                   |                   | 1120       |                   |      |
|-------------------|------------|-------------------|-------------------|------------|-------------------|------------|-------------------|-------------------|------------|-------------------|------------|-------------------|-------------------|------------|-------------------|------|
| tcc<br>Ser        | gcc<br>Ala | acc<br>Thr        | ctt<br>Leu<br>430 | cag<br>Gln | ttc<br>Phe        | cgg<br>Arg | cca<br>Pro        | ggc<br>Gly<br>435 | tat<br>Tyr | gac<br>Asp        | ggg<br>Gly | aaa<br>Lys        | acg<br>Thr<br>440 | tcc<br>Ser | atc<br>He         | 1347 |
| tcc<br>Ser        | agg<br>Arg | tgg<br>Trp<br>445 | att<br>Ile        | gtt<br>Val | gag<br>Glu        | ggg<br>Gly | cag<br>Gln<br>450 | atg<br>Met        | aga<br>Arg | cat<br>His        | caa<br>Gln | ggt<br>Gly<br>455 | gtt<br>Val        | gga<br>Gly | tta<br>Leu        | 1395 |
|                   |            |                   |                   |            |                   |            |                   |                   |            |                   |            |                   |                   | cct<br>Pro |                   | 1443 |
| aac<br>Asn<br>475 | ctc<br>Leu | gga<br>Gly        | agt<br>Ser        | ctg<br>Leu | tgg<br>Trp<br>480 | ctg<br>Leu | ctc<br>Leu        | agc<br>Ser        | ctg<br>Leu | gtg<br>Val<br>485 | tat<br>Tyr | tgg<br>Trp        | tgt<br>Cys        | tac<br>Tyr | agc<br>Ser<br>490 | 1491 |
|                   |            |                   | tgg<br>Trp        |            |                   |            |                   | tag               | ttggt      | tta g             | gttt       | tact              | gt a              | atttt      | ctat              | 1545 |
| aaag              | gaatt      | ca 1              | tatca             | atctį      | gt ta             | aatg       | gcga              | c ag              | tttt       | tgtt              | tct        | tcct              | ttg               | aattt      | tttat             | 1605 |
| atto              | ettte      | ctt †             | tctc              | tttt       | tt g              | tttc       | ttctt             | t ct              | ttgag      | gtat              | tttį       | gtaa              | tct ·             | tacte      | ggagg             | 1665 |
| gcta              | aaago      | cgt o             | cttc              | tatca      | at a              | tcga       | attgg             | g ga              | caate      | gata              | gaa        | gacaa             | atc ·             | tttgt      | tttgt             | 1725 |
| cact              | tctaa      | aag a             | aaat              | tatt       | gt a              | agat       | tttat             | t caf             | tcage      | gtat              | gaca       | attta             | aca (             | ccatt      | gatgt             | 1785 |
| aggo              | ctttt      | tta a             | aaaa              | atata      | at c              | cago       | ctgta             | a ttg             | gggt1      | taag              | atga       | attc              | ttt ·             | tctga      | atcctg            | 1845 |
| att               | toota      | agg a             | agtt              | ggtt       | tt t              | tttt       | tttta             | a aag             | gcata      | aaat              | aaat       | tttaa             | att į             | gcato      | ag                | 1902 |
|                   |            |                   |                   |            |                   |            |                   |                   |            |                   |            |                   |                   |            |                   |      |

<210> 71

<211> 245

<212> PRT

<213> Homo sapiens

<400> 71

Met Pro Val Gln Leu Ser Glu His Pro Glu Trp Asn Glu Ser Met His

1 10 15

Ser Leu Arg IIe Ser Val Gly Gly Leu Pro Val Leu Ala Ser Met Thr  $20 \hspace{1cm} 25 \hspace{1cm} 30$ 

Lys Ala Ala Asp Pro Arg Phe Arg Pro Arg Trp Lys Val IIe Leu Thr 35 40 45

Phe Phe Val Gly Ala Ala IIe Leu Trp Leu Leu Cys Ser His Arg Pro 50 55 60

Ala Pro Gly Arg Pro Pro Thr His Asn Ala His Asn Trp Arg Leu Gly 65 70 75 80

Gln Ala Pro Ala Asn Trp Tyr Asn Asp Thr Tyr Pro Leu Ser Pro Pro 85 90 95

| Gln Arg Thr Pro Ala Gly Ile Arg Tyr Arg Ile Ala Val Ile Ala Asp<br>100 105 110   |
|--|
| Leu Asp Thr Glu Ser Arg Ala Gln Glu Glu Asn Thr Trp Phe Ser Tyr<br>115 120 125   |
| Leu Lys Lys Gly Tyr Leu Thr Leu Ser Asp Ser Gly Asp Lys Val Ala<br>130 135 140   |
| Val Glu Trp Asp Lys Asp His Gly Val Leu Glu Ser His Leu Ala Glu<br>145 150 155 160   |
| Lys Gly Arg Gly Met Glu Leu Ser Asp Leu Ile Val Phe Asn Gly Lys<br>165 170 175   |
| Leu Tyr Ser Val Asp Asp Arg Thr Gly Val Val Tyr Gln ile Glu Gly<br>180 185 190   |
| Ser Lys Ala Val Pro Trp Val IIe Leu Ser Asp Gly Asp Gly Thr Val<br>195 200 205   |
| Glu Lys Gly Phe Lys Ala Glu Trp Leu Ala Val Arg Glu Ile Val Arg<br>210 215 220   |
| Lys Arg Trp Arg Leu Val Lys Gln Val Ser His Val Gly Val Leu Gly<br>225 230 235 240   |
| Gin Trp lie Gin Arg<br>245   |
| <210> 72<br><211> 1551<br><212> DNA<br><213> Homo sapiens  |
| <220><br><221> CDS<br><222> (127) (861)  |
| <400> 72<br>ggaagtcggc caccttcctc cgtcccggcc gttagcccag ccaagcccag ccaagcccag 60   |
| ccaagccccg ccgatcgcgg gcaccggagc cagccccgca gcgggtcccg cctgtctgtc 120  |
| acgctg atg ccc gtg cag ctg tct gag cac ccg gaa tgg aat gag tct  Met Pro Val Gln Leu Ser Glu His Pro Glu Trp Asn Glu Ser  1 5 10                  |
| atg cac tcc ctc cgg atc agt gtg ggg ggc ctt cct gtg ctg gcg tcc 216  Met His Ser Leu Arg Ile Ser Val Gly Gly Leu Pro Val Leu Ala Ser 15 20 25 30 |
| atg acc aag gcc gcg gac ccc cgc ttc cgc ccc cgc tgg aag gtg atc Met Thr Lys Ala Ala Asp Pro Arg Phe Arg Pro Arg Trp Lys Val Ile 35 40 45         |

| ctg acg tto<br>Leu Thr Phe        | ttt gtg<br>Phe Val            | gct<br>uly Ala                | gcc a<br>Ala l        | atc cto<br>He Lei<br>55        | tgg<br>Trp            | ctg<br>Leu        | ctc<br>Leu        | t<br>Cys<br>60    | tcc<br>Ser        | cac<br>His        | 312  |
|-----------------------------------|-------------------------------|-------------------------------|-----------------------|--------------------------------|-----------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| cgc ccg gcc<br>Arg Pro Ala<br>65  | a Pro Gly                     | agg ccc<br>Arg Pro            | ccc a<br>Pro 1<br>70  | acc cad<br>Thr His             | aat<br>s Asn          | gca<br>Ala        | cac<br>His<br>75  | aac<br>Asn        | tgg<br>Trp        | - 00              | 360  |
| ctc ggc cag<br>Leu Gly Glr<br>80  | g gog cod<br>n Ala Pro        | gcc aac<br>Ala Asr<br>85      | Trp 1                 | tac aa <sup>.</sup><br>Tyr Asi | t gac<br>n Asp        | acc<br>Thr<br>90  | tac<br>Tyr        | ccc<br>Pro        | ctg<br>Leu        |                   | 408  |
| ccc cca caa<br>Pro Pro Glr<br>95  | a agg aca<br>n Arg Thr        | ccg gct<br>Pro Ala<br>100     | ggg a                 | att cg<br>lle Ar               | g tat<br>g Tyr<br>105 | cga<br>Arg        | atc<br>lle        | gca<br>Ala        | gtt<br>Val        | atc<br>lle<br>110 | 456  |
| gca gac ctą<br>Ala Asp Lei        | g gac aca<br>u Asp Thr<br>115 | Glu Ser                       | agg g<br>Arg /        | gcc ca<br>Ala Gli<br>12        | n Glu                 | gaa<br>Glu        | aac<br>Asn        | acc<br>Thr        | tgg<br>Trp<br>125 | ttc<br>Phe        | 504  |
| agt tac ct<br>Ser Tyr Lei         | g aaa aag<br>u Lys Lys<br>130 | ggc tac<br>Gly Tyr            | Leu                   | acc ct<br>Thr Le<br>135        | g tca<br>u Ser        | gac<br>Asp        | agt<br>Ser        | ggg<br>Gly<br>140 | gac<br>Asp        | aag<br>Lys        | 552  |
| gtg gcc gtg<br>Val Ala Va<br>14   | l Glu Trp                     | g gac aaa<br>o Asp Lys        | gac o<br>Asp l<br>150 | cat gg<br>His Gl               | g gtc<br>y Val        | ctg<br>Leu        | gag<br>Glu<br>155 | tcc<br>Ser        | cac<br>His        | ctg<br>Leu        | 600  |
| gcg gag aag<br>Ala Glu Lys<br>160 | g ggg aga<br>s Gly Arg        | a ggc atg<br>g Gly Met<br>165 | : Glu I               | cta tc<br>Leu Se               | c gac<br>r Asp        | ctg<br>Leu<br>170 | att<br>He         | gtt<br>Val        | ttc<br>Phe        | aat<br>Asn        | 648  |
| ggg aaa cte<br>Gly Lys Lee<br>175 | c tac tco<br>u Tyr Sei        | gtg gat<br>Val Ası<br>180     | gac (<br>Asp /        | cgg ac<br>Arg Th               | g ggg<br>r Gly<br>185 | gtc<br>Val        | gtc<br>Val        | tac<br>Tyr        | cag<br>Gln        | atc<br>lle<br>190 | 696  |
| gaa ggc ag<br>Glu Gly Se          | c aaa goo<br>r Lys Ala<br>195 | a Val Pro                     | Trp '                 | gtg at<br>Val II<br>20         | e Leu                 | Ser               | Asp               | Gly               | Asp               | G l y             | 744  |
| acc gtg ga<br>Thr Val Gl          | g aaa ggo<br>u Lys Gly<br>210 | ttc aag<br>Phe Lys            | s Ala (               | gaa tg<br>Glu Tr<br>215        | g ctg<br>p Leu        | gca<br>Ala        | gtg<br>Val        | cgg<br>Arg<br>220 | gag<br>Glu        | att<br>He         | 792  |
| gta agg aa<br>Val Arg Ly<br>22    | s Arg Tr <sub>l</sub>         | g cgg ctg<br>o Arg Lei        | g gtg<br>u Val<br>230 | aag ca<br>Lys Gl               | a gtc<br>n Val        | tca<br>Ser        | cat<br>His<br>235 | gtc<br>Val        | ggc<br>Gly        | gtt<br>Val        | 840  |
| ctt ggc ca<br>Leu Gly Gl<br>240   |                               |                               | 3                     | gaaaat                         | gttg                  | cctt              | tt t              | ctag              | gaac              | t                 | 891  |
| gtcagaaatc                        | ctcatgo                       | ctt tcaa                      | gacttc                | tgtga                          | atgac                 | ttg               | aatt              | ttt               | tatt              | ccctgc            | 951  |
| ctagggtctg                        | tgaacga                       | ggc ctgt                      | ctcttc                | cctgg                          | ggttt                 | ctt               | tcca              | tgg               | cctt              | tatttc            | 1011 |
| tcctcttcca                        | gtgggag                       | ttt tgca                      | ggctct                | tctct                          | gtgga                 | aac               | ttca              | cga .             | gcgt              | tggctg            | 1071 |

ggcctcggct tcgctgga gtactccagg gtgaaggcag agtgggatt agacccagg 1131 tagtggagga agcgaaggaa gtgaacgctg aatgtgacgc atttctgaag agctcagctg 1191 tcaccgggca tagcctggaa gccccaagtc tgttctgact ttgcctggct gtctccttga 1251 cccgcctcct agatcattgt ccttgatgtc caggctgggt catttaaaaat agagatgcaa 1311 tcaggaaggt tgggggactt gggactgtgg ctgaattgag accttgctga tgtattcatg 1371 tcagcacctg agtcacagcc caggtgcccg gaagcagcct cttcgcatag gcagtgatt 1431 gcgattactt taaagctcac ctttttctt cccctctctg ttcgctgctg tcagcataat 1491 gattgtgttc cttccctatg ggatccatct gtttgtaaa caataaagcg tctgaggag 1551

<210> 73

<211> 352

<212> PRT

<213> Homo sapiens

<400> 73

Met Glu Ser Gly Gly Arg Pro Ser Leu Cys Gln Phe lle Leu Leu Gly
1 5 10 15

Thr Thr Ser Val Val Thr Ala Ala Leu Tyr Ser Val Tyr Arg Gln Lys 20 25 30

Ala Arg Val Ser Gln Glu Leu Lys Gly Ala Lys Lys Val His Leu Gly
35 40 45

Glu Asp Leu Lys Ser IIe Leu Ser Glu Ala Pro Gly Lys Cys Val Pro 50 55 60

Tyr Ala Val IIe Glu Gly Ala Val Arg Ser Val Lys Glu Thr Leu Asn 65 70 75 80

Ser Gln Phe Val Glu Asn Cys Lys Gly Val IIe Gln Arg Leu Thr Leu 85 90 95

Gln Glu His Lys Met Val Trp Asn Arg Thr Thr His Leu Trp Asn Asp 100 105 110

Cys Ser Lys IIe IIe His Gln Arg Thr Asn Thr Val Pro Phe Asp Leu 115 120 125

Val Pro His Glu Asp Gly Val Asp Val Ala Val Arg Val Leu Lys Pro 130 135 140

Leu Asp Ser Val Asp Leu Gly Leu Glu Thr Val Tyr Glu Lys Phe His 145 150 155 160

Pro Ser lle Gln Ser Phe Thr Asp Val lle Gly His Tyr lle Ser Gly 165 170 175

Glu Arg Pro Lys Gly Ile Gln Glu Thr Glu Glu Met Leu Lys Val Gly 180 185 190 Ala Thr Leu Thr Gly Val Gly Glu Leu Val Leu Asp Asn Asn Ser Val Arg Leu Gin Pro Pro Lys Gin Gly Met Gin Tyr Tyr Leu Ser Ser Gin Asp Phe Asp Ser Leu Leu Gln Arg Gln Glu Ser Ser Val Arg Leu Trp 225 230 Lys Val Leu Ala Leu Val Phe Gly Phe Ala Thr Cys Ala Thr Leu Phe Phe lle Leu Arg Lys Gln Tyr Leu Gln Arg Gln Glu Arg Leu Arg Leu 265 Lys Gln Met Gln Glu Glu Phe Gln Glu His Glu Ala Gln Leu Leu Ser 280 Arg Ala Lys Pro Glu Asp Arg Glu Ser Leu Lys Ser Ala Cys Val Val 295 Cys Leu Ser Ser Phe Lys Ser Cys Val Phe Leu Glu Cys Gly His Val 320 315 310 Cys Ser Cys Thr Glu Cys Tyr Arg Ala Leu Pro Glu Pro Lys Lys Cys Pro lle Cys Arg Gin Ala Ile Thr Arg Val Ile Pro Pro Tyr Asn Ser 345 <210> 74 <211> 2401 <212> DNA <213> Homo sapiens <220> <221> CDS <222> (103).. (1158) <400> 74 ttaggccggg ggggtgcggt cctggtcgga aggaggtgga gagtcggggg tcaccaggcc 60 114 tatccttggc gccacagtcg gccaccgggg ctcgccgccg tc atg gag agc gga Met Glu Ser Gly 162 ggg cgg ccc tcg ctg tgc cag ttc atc ctc ctg ggc acc acc tct gtg Gly Arg Pro Ser Leu Cys Gln Phe lle Leu Leu Gly Thr Thr Ser Val gtc acc gcc gcc ctg tac tcc gtg tac cgg cag aag gcc cgg gtc tcc Val Thr Ala Ala Leu Tyr Ser Val Tyr Arg Gln Lys Ala Arg Val Ser 210 caa gag ctc aag gga gct aaa aaa gtt cat ttg ggt gaa gat tta aag 258 Gin Glu Leu Lys Gly Ala Lys Lys Val His Leu Gly Glu Asp Leu Lys

| agt<br>Ser        | att<br>lle        | cti<br>Leu<br>55  | ı Ser             | a gaa<br>Glu      | gct<br>Ala        | cca<br>Pro        | gga<br>Gly<br>60  | Lys               | tgo<br>Cys        | c gtg<br>s Val    | g cct<br>I Pro    | t tat<br>o Tyr<br>65 | Ala               | gti<br>a Val      | ata<br>He         | 306 |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|----------------------|-------------------|-------------------|-------------------|-----|
| gaa<br>Glu        | gga<br>Gly<br>70  | Ala               | gtg<br>a Val      | g cgg<br>Arg      | tct<br>Ser        | gtt<br>Val<br>75  | Lys               | gaa<br>Glu        | acg<br>Thr        | ctt<br>Leu        | aad<br>Asr<br>80  | Ser                  | cag<br>Glr        | g ttt<br>1 Phe    | gtg<br>Val        | 354 |
| gaa<br>Glu<br>85  | Asn               | tgc<br>Cys        | aag<br>Lys        | ggg<br>Gly        | gta<br>Val<br>90  | Пe                | cag<br>G n        | cgg<br>Arg        | ctg<br>Leu        | aca<br>Thr<br>95  | Leu               | cag<br>Glr           | gag<br>Glu        | g cac<br>His      | aag<br>Lys<br>100 | 402 |
| atg<br>Met        | gtg<br>Val        | tgg<br>Trp        | aat<br>Asn        | cga<br>Arg<br>105 | acc<br>Thr        | acc<br>Thr        | cac<br>His        | ctt<br>Leu        | tgg<br>Trp<br>110 | Asn               | gat<br>Asp        | tgc<br>Cys           | tca<br>Ser        | aag<br>Lys<br>115 | atc               | 450 |
| att<br>He         | cat<br>His        | cag<br>Gln        | agg<br>Arg<br>120 | acc<br>Thr        | aac<br>Asn        | aca<br>Thr        | gtg<br>Val        | ccc<br>Pro<br>125 | ttt<br>Phe        | gac<br>Asp        | ctg<br>Leu        | gtg<br>Val           | Pro<br>130        | His               | gag<br>Glu        | 498 |
| gat<br>Asp        | ggc<br>Gly        | gtg<br>Val<br>135 | Asp               | gtg<br>Val        | gct<br>Ala        | gtg<br>Val        | cga<br>Arg<br>140 | gtg<br>Val        | ctg<br>Leu        | aag<br>Lys        | ccc<br>Pro        | ctg<br>Leu<br>145    | gac<br>Asp        | tca<br>Ser        | gtg<br>Val        | 546 |
| gat<br>Asp        | ctg<br>Leu<br>150 | ggt<br>Gly        | cta<br>Leu        | gag<br>Glu        | act<br>Thr        | gtg<br>Val<br>155 | tat<br>Tyr        | gag<br>Glu        | aag<br>Lys        | ttc<br>Phe        | cac<br>His<br>160 | Pro                  | tcg<br>Ser        | att<br>lle        | cag<br>G n        | 594 |
| tcc<br>Ser<br>165 | ttc<br>Phe        | acc<br>Thr        | gat<br>Asp        | gtc<br>Val        | atc<br>  e<br>170 | ggc<br>Gly        | cac<br>His        | tac<br>Tyr        | atc<br>lle        | agc<br>Ser<br>175 | ggt<br>Gly        | gag<br>Glu           | cgg<br>Arg        | ccc<br>Pro        | aaa<br>Lys<br>180 | 642 |
| ggc<br>Gly        | atc<br>He         | caa<br>Gln        | gag<br>Glu        | acc<br>Thr<br>185 | gag<br>Glu        | gag<br>Glu        | atg<br>Met        | ctg<br>Leu        | aag<br>Lys<br>190 | gtg<br>Val        | ggg<br>Gly        | gcc<br>Ala           | acc<br>Thr        | ctc<br>Leu<br>195 | aca<br>Thr        | 690 |
| ggg<br>Gly        | gtt<br>Val        | ggc<br>Gly        | gaa<br>Glu<br>200 | ctg<br>Leu        | gtc<br>Val        | ctg<br>Leu        | gac<br>Asp        | aac<br>Asn<br>205 | aac<br>Asn        | tct<br>Ser        | gtc<br>Val        | cgc<br>Arg           | ctg<br>Leu<br>210 | cag<br>Gln        | ccg<br>Pro        | 738 |
| ccc<br>Pro        | aaa<br>Lys        | caa<br>Gln<br>215 | ggc<br>Gly        | atg<br>Met        | cag<br>Gln        | tac<br>Tyr        | tat<br>Tyr<br>220 | cta<br>Leu        | agc<br>Ser        | agc<br>Ser        | cag<br>Gln        | gac<br>Asp<br>225    | ttc<br>Phe        | gac<br>Asp        | agc<br>Ser        | 786 |
| Leu               | ctg<br>Leu<br>230 | cag<br>Gln        | agg<br>Arg        | cag<br>Gln        | Glu               | tcg<br>Ser<br>235 | agc<br>Ser        | gtc<br>Val        | agg<br>Arg        | ctc<br>Leu        | tgg<br>Trp<br>240 | aag<br>Lys           | gtg<br>Val        | ctg<br>Leu        | gcg<br>Ala        | 834 |
| ctg<br>Leu<br>245 | gtt<br>Val        | ttt<br>Phe        | ggc<br>Gly        | ttt<br>Phe        | gcc<br>Ala<br>250 | aca<br>Thr        | tgt<br>Cys        | gcc<br>Ala        | acc<br>Thr        | ctc<br>Leu<br>255 | ttc<br>Phe        | ttc<br>Phe           | att<br>Ile        | ctc<br>Leu        | cgg<br>Arg<br>260 | 882 |
| aag<br>Lys        | cag<br>Gln        | tat<br>Tyr        | Leu               | cag<br>Gln<br>265 | cgg<br>Arg        | cag<br>Gln        | gag<br>Glu        | Arg               | ctg<br>Leu<br>270 | cgc<br>Arg        | ctc<br>Leu        | aag<br>Lys           | cag<br>Gln        | atg<br>Met<br>275 | cag<br>Gln        | 930 |

| gag gag ttc cag gag et gag gcc cag ctg ctg agc cga gag cct 978<br>Glu Glu Phe Gln Glu His Glu Ala Gln Leu Leu Ser Arg Ala Lys Pro<br>280 285 290           |
|--|
| gag gac agg gag agt ctg aag agc gcc tgt gta gtg tgt ctg agc agc 1026<br>Glu Asp Arg Glu Ser Leu Lys Ser Ala Cys Val Val Cys Leu Ser Ser<br>295 300 305     |
| ttc aag tcc tgc gtc ttt ctg gag tgt ggg cac gtt tgt tcc tgc acc 1074 Phe Lys Ser Cys Val Phe Leu Glu Cys Gly His Val Cys Ser Cys Thr 310 315 320           |
| gag tgc tac cgc gcc ttg cca gag ccc aag aag tgc cct atc tgc aga 1122<br>Glu Cys Tyr Arg Ala Leu Pro Glu Pro Lys Lys Cys Pro lle Cys Arg<br>325 330 335 340 |
| cag gcg atc acc cgg gtg ata ccc ccg tac aac agc taatagtttg 1168 Gln Ala lle Thr Arg Val lle Pro Pro Tyr Asn Ser 345 350                                    |
| gaagccgcac agcttgacct ggaagcaccc ctgccccctt ttcagggatt tttatctcga 1228   |
| ggcctttgga ggagcagtgg tgggggtagc tgtcacctcc aggtatgatt gagggaggaa 1288   |
| tcgggtagaa actctccaga cccatgcctc caatggcagg atgctgcctt tcccacctga 1348   |
| gaggggaccc tgtccatgtg cagcctcatc agagcctcac cctgggagga tgccgtggcg 1408   |
| tctcctccca ggagccagat cagtgcgagt gtgactgaaa atgcctcatc acttaagcac 1468   |
| caaagccagt gatcagcagc tcttctgttc ctgtgtcttc tgtttttttc tggtgaatcg 1528   |
| ttgcttgctg tggacttggt ggaggactca gaggggagga aaggctgggc cccgagtaca 1588   |
| acggatgcct tgggtgctgc ctccgaagag actctgccgc agcttttctt cttttcctc 1648  |
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| tgaagtcagc acatccgctt ctgcccagat ggtcggggcc ccgggcaaca gattgaagag 1828   |
| agatcatgtg aagggcagtt ggtcaggcag gcctcctggt ttcgccactg gccctgattt 1888   |
| gaactcctgc cacttgggag agctcggggt ggtccctggt tttccctcct ggagaatgag 1948   |
| gcgcagaggc ctcgcctcct gaaggacgca gtgtggatgc cactggccta gtgtcctggc 2008   |
| ctcacagctt ccttgcaagg ctgtcacaag gaaaagcagc cggctggcac cctgagcata 2068   |
| tgccctcttg gggctccctc atccagcccg tcgcagcttt gacatcttgg tgtactcatg 2128   |
| togottotoc ttgtgttacc coctoccagt attaccattt goccotcacc tgcccttggt 2188   |
| gagcctttta gtgcaagaca gatggggctg ttttccccca cctctgagta gttggaggtc 2248   |
| acatacacag ctctttttt attgcccttt tctgcctctg aatgttcatc tctcgtcctc 2308  |

<210> 75

<211> 352

<212> PRT

<213> Homo sapiens

<400> 75

Met Glu Ser Gly Gly Arg Pro Ser Leu Cys Gln Phe lle Leu Leu Gly

Thr Thr Ser Val Val Thr Ala Ala Leu Tyr Ser Val Tyr Arg Gln Lys

Ala Arg Val Ser Gln Glu Leu Lys Gly Ala Lys Lys Val His Leu Gly

Glu Asp Leu Lys Ser lie Leu Ser Glu Ala Pro Gly Lys Cys Val Pro

Tyr Ala Val Ile Glu Gly Ala Val Arg Ser Val Lys Glu Thr Leu Asn

Ser Gln Phe Val Glu Asn Cys Lys Gly Val Ile Gln Arg Leu Thr Leu

Gln Glu His Lys Met Val Trp Asn Arg Thr Thr His Leu Trp Asn Asp 100

Cys Ser Lys IIe IIe His Gln Arg Thr Asn Thr Val Pro Phe Asp Leu

Val Pro His Glu Asp Gly Val Asp Val Ala Val Arg Val Leu Lys Pro

Leu Asp Ser Val Asp Leu Gly Leu Glu Thr Val Tyr Glu Lys Phe His 145 160

Pro Ser Ile Gln Ser Phe Thr Asp Val Ile Gly His Tyr Ile Ser Gly

Glu Arg Pro Lys Gly Ile Gln Glu Thr Glu Glu Met Leu Lys Val Gly

Ala Thr Leu Thr Gly Val Gly Glu Leu Val Leu Asp Asn Asn Ser Val

Arg Leu Gln Pro Pro Lys Gln Gly Met Gln Tyr Tyr Leu Ser Ser Gln

Asp Phe Asp Ser Leu Leu Gln Arg Gln Glu Ser Ser Val Arg Leu Trp

Lys Val Leu Ala Leu Val Phe Gly Phe Ala Thr Cys Ala Thr Leu Phe 250

|   | Πe   | : Le                       | u Ar.<br>26   | g Ly<br>O   | s Gli   | n Ty   | r Lei   | u G1;<br>26  | n Arg<br>5                                   | g Glr   | n Glu                                 | ı Arg   | : Leu<br>270                             |  | g Leu  |   |
|---|--|----------------------------|---|---|---|--|---|--|--|---|---------------------------------------|---|--|--|--|---|
| Lys   | Gln  | Me <sup>-</sup><br>27      | t Gli   | n Gli   | u Gli   | u Phe  | e Gir<br>280  | n Glu<br>O   | u His  | s Glu   | ıAla                                  | Gin<br>285  |  | Lei  | . Ser  |   |
| Arg   | Ala<br>290                                       | Lys                        | s Pro   | o Gli   | ı Asp   | 295  | g Glu   | u Sei  | Leu  | ı Lys   | Ser<br>300                            | Ala   | Cys                                      | Val  | Val  |   |
| Cys<br>305  | Leu  | Ser                        | Sei   | · Phe   | 2 Lys<br>31(  | s Ser<br>)   | Cys   | s Val  | Phe  | Leu<br>315  | Glu                                   | Cys   | Gly                                      | His  | Val<br>320   |   |
| Cys   | Ser  | Cys                        | 5 Thr   | Glu<br>325  | ı Cys   | Tyr  | · Arg   | g Ala  | Leu<br>330                                   | Pro   | Glu                                   | Pro   | Lys                                      | Lys<br>335                                     |  |   |
| Pro   | lle  | Cys                        | 340   | g Glr   | ı Ala   | lle  | . Thr   | Arg<br>345   | , Val  | lle   | Pro                                   | Leu   | Tyr<br>350                               | Asn  | Ser  |   |
| <220<br><221  | > 24<br>  2 > DI<br>  3 > Ho<br>  > CI           | 401<br>NA<br>omo           | sapi  |   |   |  |   |  |  |   |                                       |   |  |  |  |   |
| <222<br><400  | !> (1<br>!> <b>76</b>                            |                            | (1  | 158)  |   |  |   |  |  |   |                                       |   |  |  |  |   |
|   |  | ,                          |   |   |   |  |   |  |  |   |                                       |   |  |  |  |   |
| ttag  |  | gg                         |   |   |   |  |   |  |  |   |                                       |   |  |  | cagged   | : 60  |
| ttag  |  | gg                         |   |   |   |  |   |  | gaggt  |   | tc a                                  |   | ag a                                     | gc g   | gga  | : 60<br>114   |
| ttag  | cttg<br>cgg                                      | gg ;                       | gcca<br>tcg   | cagto<br>ctg  | cg go   | ccaco  | cgggg<br>ttc  | g cto<br>atc   | cgccg  | gccg  | tc a                                  | itg g<br>let G<br>1   | ag a                                     | gc g<br>er (                                   | gga<br>Ny  |   |
| tatc<br>ggg<br>Gly  | cttg<br>cgg<br>Arg                               | gg gcc                     | tcg<br>Ser  | cagto<br>ctg<br>Leu<br>ctg                            | tgc<br>Cys<br>10                                    | cag<br>Gin<br>tcc                                      | ttc<br>Phe  | atc  | ctc<br>Leu                                   | ctg<br>Leu<br>15  | tc a<br>M<br>ggc<br>Gly               | etg g<br>let G<br>1<br>acc<br>Thr                               | ag a<br>lu S<br>acc<br>Thr               | gc g<br>er (<br>tct<br>Ser                     | gga<br>Gly<br>gtg<br>Val<br>20                             | 114   |
| tag<br>tatc<br>ggg<br>Gly /<br>5<br>gtc a                       | cttg<br>cgg<br>Arg<br>acc<br>Thr                 | gg gc gcc<br>Progcc<br>Ala | tcg<br>Ser<br>gcc<br>Ala                                    | ctg<br>Leu<br>ctg<br>Leu<br>25                        | tgc<br>Cys<br>10<br>tac<br>Tyr                      | cag<br>Gin<br>tcc<br>Ser                               | ttc<br>Phe<br>gtg<br>Val  | atc<br> le<br>tac<br>Tyr                                   | ctc<br>Leu<br>cgg<br>Arg<br>30               | ctg<br>Leu<br>15<br>cag<br>Gln                            | tc a<br>M<br>ggc<br>Gly<br>aag<br>Lys | tg g<br>let G<br>acc<br>Thr<br>gcc<br>Ala                       | ag a<br>lu S<br>acc<br>Thr<br>cgg<br>Arg | tct<br>Ser<br>gtc<br>Val                       | gga<br>gtg<br>Val<br>20<br>tcc<br>Ser                      | 114<br>162  |
| ttag tatc  ggg Gly 5 gtc a Val                                  | cttg<br>cgg<br>Arg<br>acc<br>Thr<br>gag          | ggg ; ccc ; ccc Pro        | tcg<br>Ser<br>gcc<br>Ala<br>aag<br>Lys<br>40                | cagto<br>ctg<br>Leu<br>ctg<br>Leu<br>25<br>gga<br>Gly | tgc<br>Cys<br>10<br>tac<br>Tyr<br>gct<br>Ala        | cag<br>Gin<br>tcc<br>Ser<br>aaa<br>Lys                 | ttc<br>Phe<br>gtg<br>Val<br>aaa<br>Lys                            | atc<br>lle<br>tac<br>Tyr<br>gtt<br>Val<br>45               | ctc<br>Leu<br>cgg<br>Arg<br>30<br>cat<br>His | ctg<br>Leu<br>15<br>cag<br>Gln<br>ttg<br>Leu              | ggc<br>Gly<br>aag<br>Lys              | tg g<br>let G<br>1<br>acc<br>Thr<br>gcc<br>Ala<br>gaa<br>Glu    | ag a<br>lu S<br>acc<br>Thr<br>cgg<br>Arg | tct<br>Ser<br>gtc<br>Val<br>35<br>tta<br>Leu   | gga<br>Bly<br>gtg<br>Val<br>20<br>tcc<br>Ser<br>aag<br>Lys | 114<br>162<br>210   |
| ttag tatc  ggg Gly 5 gtc aval caa g Gln agt a Ser l gaa g Glu G | cttg<br>cgg<br>Arg<br>acc<br>Thr<br>gag<br>att ( | ccc Progcc Alacteuctt      | tcg<br>Ser<br>gcc<br>Ala<br>aag<br>Lys<br>tca<br>Ser<br>gtg | cagto<br>ctg<br>Leu<br>ctg<br>Leu<br>25<br>gga<br>Gly | tgc<br>Cys<br>10<br>tac<br>Tyr<br>gct<br>Ala<br>gct | ccace<br>Gin<br>tcc<br>Ser<br>aaa<br>Lys<br>cca<br>Pro | ttc<br>Phe<br>gtg<br>Val<br>aaa<br>Lys<br>gga<br>Gly<br>60<br>aaa | atc<br>lle<br>tac<br>Tyr<br>gtt<br>Val<br>45<br>aaa<br>Lys | ctc<br>Leu<br>cgg<br>Arg<br>30<br>cat<br>His | ctg<br>Leu<br>15<br>cag<br>Gln<br>ttg<br>Leu<br>gtg Val I | ggc<br>Gly<br>aag<br>Lys              | tg glet G<br>1<br>acc<br>Thr<br>gcc<br>Ala<br>gaa<br>Glu<br>tat | ag ag ag lu S acc Thr cgg Arg gat Asp 50 | tct<br>Ser<br>gtc<br>Val<br>ttau<br>gtt<br>Val | gga<br>gtg<br>Val<br>20<br>tcc<br>Ser<br>aag<br>Lys        | <ul><li>114</li><li>162</li><li>210</li><li>258</li></ul> |

| 85         |            |            |                   |                   | 0          |            |            |                   |                   | 95         |            |            |                   |                   | 100        |      |
|------------|------------|------------|-------------------|-------------------|------------|------------|------------|-------------------|-------------------|------------|------------|------------|-------------------|-------------------|------------|------|
| atg<br>Met | gtg<br>Val | tgg<br>Trp | aat<br>Asn        | cga<br>Arg<br>105 | acc<br>Thr | acc<br>Thr | cac<br>His | ctt<br>Leu        | tgg<br>Trp<br>110 | aat<br>Asn | gat<br>Asp | tgc<br>Cys | tca<br>Ser        | aag<br>Lys<br>115 | atc<br>Ile | 450  |
| att<br>He  | cat<br>His | cag<br>Gln | agg<br>Arg<br>120 | acc<br>Thr        | aac<br>Asn | aca<br>Thr | gtg<br>Val | ccc<br>Pro<br>125 | ttt<br>Phe        | gac<br>Asp | ctg<br>Leu | gtg<br>Val | ccc<br>Pro<br>130 | cac<br>His        | gag<br>Glu | 498  |
|            |            |            | gat<br>Asp        |                   |            |            |            |                   |                   |            |            |            |                   |                   |            | 546  |
|            |            |            | cta<br>Leu        |                   |            |            |            |                   |                   |            |            |            |                   |                   |            | 594  |
|            |            |            | gat<br>Asp        |                   |            |            |            |                   |                   |            |            |            |                   |                   |            | 642  |
|            |            |            | gag<br>Glu        |                   |            |            |            |                   |                   |            |            |            |                   |                   |            | 690  |
|            |            |            | gaa<br>Glu<br>200 |                   |            |            |            |                   |                   |            |            |            |                   |                   |            | 738  |
|            |            |            | ggc<br>Gly        |                   |            |            |            |                   |                   |            |            |            |                   |                   |            | 786  |
|            |            |            | agg<br>Arg        |                   |            |            |            |                   |                   |            |            |            |                   |                   |            | 834  |
|            |            |            | ggc<br>Gly        |                   |            |            |            |                   |                   |            |            |            |                   |                   |            | 882  |
|            |            |            | ctg<br>Leu        |                   |            |            |            |                   |                   |            |            |            |                   |                   |            | 930  |
|            |            |            | cag<br>Gln<br>280 |                   |            |            |            |                   |                   |            |            |            |                   |                   |            | 978  |
|            |            |            | gag<br>Glu        |                   |            |            |            |                   |                   |            |            |            |                   |                   |            | 1026 |
| Phe        |            |            | tgc<br>Cys        |                   |            |            |            |                   |                   |            |            |            |                   |                   |            | 1074 |

gag tgc tac cgc gc gg cca gag ccc aag aag tgc cct tgc aga 1122 Glu Cys Tyr Arg Ala Leu Pro Glu Pro Lys Lys Cys Pro Tie Cys Arg 325 330 335 340

cag gcg atc acc cgg gtg ata ccc ctg tac aac agc taatagtttg 1168 Gin Ala ile Thr Arg Val ile Pro Leu Tyr Asn Ser 345 350

gaagccgcac agcttgacct ggaagcaccc ctgccccctt ttcagggatt tttatctcga 1228 ggcctttgga ggagcagtgg tgggggtagc tgtcacctcc aggtatgatt gagggaggaa 1288 tcgggtagaa actctccaga cccatgcctc caatggcagg atgctgcctt tcccacctga 1348 gaggggaccc tgtccatgtg cagcctcatc agagcctcac cctgggagga tgccgtggcg 1408 tctcctccca ggagccagat cagtgcgagt gtgactgaaa atgcctcatc acttaagcac 1468 caaagccagt gatcagcagc tottotgtto otgtgtotto tgttttttto tggtgaatcg 1528 ttgcttgctg tggacttggt ggaggactca gaggggagga aaggctgggc cccgagtaca 1588 acggatgcct tgggtgctgc ctccgaagag actctgccgc agcttttctt ctttttcctc 1648 atgccccggg aaacagtctt tcttcagaat tgtcaggctg ggcaggtcaa cttgtgttcc 1708 tttcccctca cctgcttgcc tccttaacgc ctgcacgtgt gtgtagagga caaaagaaag 1768 tgaagtcagc acatccgctt ctgcccagat ggtcggggcc ccgggcaaca gattgaagag 1828 agatcatgtg aagggcagtt ggtcaggcag gcctcctggt ttcgccactg gccctgattt 1888 gaactcctgc cacttgggag agctcggggt ggtccctggt tttccctcct ggagaatgag 1948 gcgcagaggc ctcgcctcct gaaggacgca gtgtggatgc cactggccta gtgtcctggc 2008 ctcacagctt ccttgcaagg ctgtcacaag gaaaagcagc cggctggcac cctgagcata 2068 tgccctcttg gggctccctc atccagcccg tcgcagcttt gacatcttgg tgtactcatg 2128 togottotoc ttgtgttacc coctoccagt attaccattt gcccctcacc tgcccttggt 2188 gagcctttta gtgcaagaca gatggggctg ttttccccca cctctgagta gttggaggtc 2248 acatacacag ctctttttt attgcccttt tctgcctctg aatgttcatc tctcgtcctc 2308 ctttgtgcag gcgaggaagg ggtgccctca ggggccgaca ctagtgtgat gcagtgtcca 2368 gtgtgaacag cagaaattaa acatgttgca acc 2401

<sup>&</sup>lt;210> 77 <211> 697 <212> PRT

<sup>/212&</sup>gt; Hama

<sup>&</sup>lt;213> Homo sapiens

<sup>&</sup>lt;400> 77
Met Cys Lys Ser Leu Arg Tyr Cys Phe Ser His Cys Leu Tyr Leu Ala



Met Thr Arg Leu Glu Glu Val Asn Arg Glu Val Asn Met His Ser Ser 20 25 30

Val Arg Tyr Leu Gly Tyr Leu Ala Arg Ile Asn Leu Leu Val Ala Ile 35 40 45

Cys Leu Gly Leu Tyr Val Arg Trp Glu Lys Thr Ala Asn Ser Leu lle 50 55 60

Leu Val lle Phe lle Leu Gly Leu Phe Val Leu Gly lle Ala Ser lle 65 70 75 80

Leu Tyr Tyr Phe Ser Met Glu Ala Ala Ser Leu Ser Leu Ser Asn 85 90 95

Leu Trp Phe Gly Phe Leu Leu Gly Leu Leu Cys Phe Leu Asp Asn Ser 100 105 110

Ser Phe Lys Asn Asp Val Lys Glu Glu Ser Thr Lys Tyr Leu Leu Leu 115 120 125

Thr Ser IIe Val Leu Arg IIe Leu Cys Ser Leu Val Glu Arg IIe Ser 130 135 140

Gly Tyr Val Arg His Arg Pro Thr Leu Leu Thr Thr Val Glu Phe Leu 145 150 155 160

Glu Leu Val Gly Phe Ala IIe Ala Ser Thr Thr Met Leu Val Glu Lys 165 170 175

Ser Leu Ser Val IIe Leu Leu Val Val Ala Leu Ala Met Leu IIe IIe 180 185 190

Asp Leu Arg Met Lys Ser Phe Leu Ala IIe Pro Asn Leu Val IIe Phe 195 200 205

Ala Val Leu Leu Phe Phe Ser Ser Leu Glu Thr Pro Lys Asn Pro Ile 210 215 220

Ala Phe Ala Cys Phe Phe lle Cys Leu lle Thr Asp Pro Phe Leu Asp 225 230 235 240

lle Tyr Phe Ser Gly Leu Ser Val Thr Glu Arg Trp Lys Pro Phe Leu 245 250 255

Tyr Arg Gly Arg Ile Cys Arg Arg Leu Ser Val Val Phe Ala Gly Met 260 265 270

lle Glu Leu Thr Phe Phe lle Leu Ser Ala Phe Lys Leu Arg Asp Thr 275 280 285

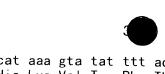
His Leu Trp Tyr Phe Val IIe Pro Gly Phe Ser IIe Phe Gly IIe Phe 290 295 300

Trp Met Ile Cys His Ile Ile Phe Leu Leu Thr Leu Trp Gly Phe His 305 310 315 320

| Th                    | r Ly       | s Le       | eu As      | n As<br>32   | p oys      | s His       | s Ly:        | s Va        | Tyı<br>330 | Phe        | e Thr        | - His      | s Ar        | g Th<br>33  | r Asp<br>5 |
|-----------------------|------------|------------|------------|--------------|------------|-------------|--------------|-------------|------------|------------|--------------|------------|-------------|-------------|------------|
| Ту                    | r As       | n Se       | r Le<br>34 | u As<br>0    | p Arg      | g Ile       | e Met        | t Ala<br>34 | a Ser<br>5 | Lys        | s Gly        | / Met      | t Ar.<br>35 |             | s Phe      |
| Су                    | s Le       | u   <br>35 | e Se<br>5  | r Gli        | u Glr      | Lei         | u Va∜<br>360 | l Phe       | e Phe      | e Sei      | Lei          | Lei<br>365 | ı Ala<br>5  | a Th        | r Ala      |
| 110                   | e Le<br>37 | u G1<br>O  | y Al       | a Va         | l Ser      | 7rp<br>375  | Glr          | ı Pro       | Thr        | . Asr      | 1 Gly<br>380 | '   ∈<br>  | e Phe       | e Lei       | u Ser      |
| Ме <sup>з</sup><br>38 | t Pho      | e Le       | u II       | e Va         | Leu<br>390 | Pro         | Leu          | Glu         | ı Ser      | Met<br>395 | Ala          | His        | s Gly       | / Lei       | Phe 400    |
| His                   | s Gli      | ı Le       | u Gl       | y Asr<br>405 | Cys        | Leu         | ı Gly        | Gly         | Thr<br>410 | Ser        | Val          | Gly        | ' Tyr       | Ala<br>415  |            |
| Val                   | He         | e Pr       | o Th       | r Asr<br>O   | Phe        | Cys         | Ser          | Pro<br>425  | Asp        | Gly        | Gln          | Pro        | Thr<br>430  |             | ı Leu      |
| Pro                   | Pro        | 43!        | u His<br>5 | s Val        | Gln        | Glu         | Leu<br>440   | Asn         | Leu        | Arg        | Ser          | Thr<br>445 | Gly         | Met         | Leu        |
| Asn                   | 450        | alle<br>)  | e Glr      | n Arg        | Phe        | Phe<br>455  | Ala          | Tyr         | His        | Met        | lle<br>460   | Glu        | Thr         | Tyr         | Gly        |
| Cys<br>465            | Asp        | Туг        | Ser        | Thr          | Ser<br>470 | Gly         | Leu          | Ser         | Phe        | Asp<br>475 | Thr          | Leu        | His         | Ser         | Lys<br>480 |
| Leu                   | Lys        | Ala        | a Phe      | Leu<br>485   | Glu        | Leu         | Arg          | Thr         | Val<br>490 | Asp        | Gly          | Pro        | Arg         | His<br>495  | Asp        |
| Thr                   | Tyr        | He         | Leu<br>500 | Tyr          | Tyr        | Ser         | Gly          | His<br>505  | Thr        | His        | Gly          | Thr        | Gly<br>510  | Glu         | Trp        |
| Ala                   | Leu        | Ala<br>515 | Gly        | Gly          | Asp        | Thr         | Leu<br>520   | Arg         | Leu        | Asp        | Thr          | Leu<br>525 | lle         | Glu         | Trp        |
| Trp                   | Arg<br>530 | Glu        | Lys        | Asn          | Gly        | Ser<br>535  | Phe          | Cys         | Ser        | Arg        | Leu<br>540   | lle        | He          | Val         | Leu        |
| Asp<br>545            | Ser        | Glu        | Asn        | Ser          | Thr<br>550 | Pro         | Trp          | Val         | Lys        | G1u<br>555 | Val          | Arg        | Lys         | He          | Asn<br>560 |
| Asp                   | Gln        | Tyr        | ile        | Ala<br>565   | Val        | Gln         | Gly          | Ala         | G1u<br>570 | Leu        | He           | Lys        | Thr         | Va I<br>575 | Asp        |
| lle                   | Glu        | Glu        | Ala<br>580 | Asp          | Pro        | Pro         | Gln          | Leu<br>585  | Gly        | Asp        | Phe          |            | Lys<br>590  | Asp         | Trp        |
| Val                   | Glu        | Tyr<br>595 | Asn        | Cys          | Asn :      | Ser         | Ser<br>600   | Asn         | Asn        | lle        |              | Trp<br>605 | Thr         | Glu         | Lys        |
| Gly                   | Arg<br>610 | Thr        | Val        | Lys          | Ala Y      | Val.<br>315 | Tyr          | Gly         | Val:       | Ser        | Lys .<br>620 | Arg        | Trp         | Ser         | Asp        |

| Tyr Thr Leu His Leu Thr Gly Ser Asp Val Ala Lys Herr Met 625 630 635 640  |
|---|
| Leu His Phe Pro Arg Ile Thr Tyr Pro Leu Val His Leu Ala Asn Trp<br>645 650 655  |
| Leu Cys Gly Leu Asn Leu Phe Trp Ile Cys Lys Thr Cys Phe Arg Cys 660 665 670   |
| Leu Lys Arg Leu Lys Met Ser Trp Phe Leu Pro Thr Val Leu Asp Thr<br>675 680 685  |
| Gly Gln Gly Phe Lys Leu Val Lys Ser<br>690 695  |
| <210> 78<br><211> 3008<br><212> DNA<br><213> Homo sapiens   |
| <220><br><221> CDS<br><222> (372) (2462)  |
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| aaagtttacg ccgacactgg cctgtattag cgcgtatggc ctcgggccct cgttcccaa 120  |
| ggcgtgccgc ctccctgttc tcagtcgcag gctgaagcct tgtctgctct cctcctttt 180  |
| ggtttggttt tggaactgac tccgagggtt gggagagcgc gttggtggcg acggccgagt 240   |
| cagatcacta taaacaaaat ttccacaaga gaaaatgttg aaataggagt tgcggataca 300   |
| ttggatatac tggatgaaat acaagcggtt aatttttgta acgtgaggga aaagcccaca 360   |
| ttgctggtta c atg tgt aaa tca ctg cgt tat tgc ttt agt cat tgt ctc 410<br>Met Cys Lys Ser Leu Arg Tyr Cys Phe Ser His Cys Leu<br>1 5 10                 |
| tat tta gca atg aca aga ctg gaa gaa gta aat aga gaa gtg aac atg 458<br>Tyr Leu Ala Met Thr Arg Leu Glu Glu Val Asn Arg Glu Val Asn Met<br>15 20 25    |
| cat tot toa gtg cgg tat ott ggc tat tta gcc aga atc aat tta ttg 506<br>His Ser Ser Val Arg Tyr Leu Gly Tyr Leu Ala Arg Ile Asn Leu Leu<br>30 35 40 45 |
| gtt gct ata tgc tta ggt cta tac gta aga tgg gaa aaa aca gca aat 554<br>Val Ala Ile Cys Leu Gly Leu Tyr Val Arg Trp Glu Lys Thr Ala Asn<br>50 55 60    |
| tcc tta att ttg gta att ttt att ctt ggt ctt ttt gtt ctt gga atc Ser Leu IIe Leu Val IIe Phe IIe Leu Gly Leu Phe Val Leu Gly IIe 65 70 75              |

| gcc<br>Ala        | ago<br>Ser        | ata<br>Ile<br>80  | Leu               | tat<br>ı Tyr      | Tyr               | tat<br>Tyr        | ttt<br>Phe<br>85  | : Ser             | atg<br>Met         | gaa<br>Glu        | a gca<br>ı Ala    | gca<br>Ala<br>90  | Ser               | ta<br>Leu         | agt<br>Ser        | 650  |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|--------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| ctc<br>Leu        | tcc<br>Ser<br>95  | Asn               | ctt<br>Leu        | tgg<br>Trp        | ttt<br>Phe        | gga<br>Gly<br>100 | Phe               | ttg<br>Leu        | ctt<br>Leu         | ggc               | cto<br>Leu<br>105 | Leu               | tgt<br>Cys        | ttt<br>Phe        | ctt<br>Leu        | 698  |
| gat<br>Asp<br>110 | Asn               | tca<br>Ser        | tcc<br>Ser        | ttt<br>Phe        | aaa<br>Lys<br>115 | Asn               | gat<br>Asp        | gta<br>Val        | aaa<br>Lys         | gaa<br>Glu<br>120 | ıGlu              | tca<br>Ser        | acc<br>Thr        | aaa<br>Lys        | tat<br>Tyr<br>125 | 746  |
| ttg<br>Leu        | ctt<br>Leu        | cta<br>Leu        | aca<br>Thr        | tcc<br>Ser<br>130 | Пe                | gtg<br>Val        | tta<br>Leu        | agg<br>Arg        | ata<br>Ile<br>135  | Leu               | tgc<br>Cys        | tct<br>Ser        | ctg<br>Leu        | gtg<br>Val<br>140 | Glu               | 794  |
| aga<br>Arg        | att<br>He         | tct<br>Ser        | ggt<br>Gly<br>145 | tat<br>Tyr        | gtc<br>Val        | cgt<br>Arg        | cat<br>His        | cgg<br>Arg<br>150 | ccc<br>Pro         | act<br>Thr        | tta<br>Leu        | cta<br>Leu        | acc<br>Thr<br>155 | Thr               | gtt<br>Val        | 842  |
| gaa<br>Glu        | ttt<br>Phe        | ctg<br>Leu<br>160 | gag<br>Glu        | ctt<br>Leu        | gtt<br>Val        | gga<br>Gly        | ttt<br>Phe<br>165 | gcc<br>Ala        | att<br>He          | gcc<br>Ala        | agc<br>Ser        | aca<br>Thr<br>170 | act<br>Thr        | atg<br>Met        | ttg<br>Leu        | 890  |
| gtg<br>Val        | gag<br>Glu<br>175 | aag<br>Lys        | tct<br>Ser        | ctg<br>Leu        | agt<br>Ser        | gtc<br>Val<br>180 | att<br>He         | ttg<br>Leu        | ctt<br>Leu         | gtt<br>Val        | gta<br>Val<br>185 | gct<br>Ala        | ctg<br>Leu        | gct<br>Ala        | atg<br>Met        | 938  |
| ctg<br>Leu<br>190 | att<br>He         | att<br>He         | gat<br>Asp        | ctg<br>Leu        | aga<br>Arg<br>195 | atg<br>Met        | aaa<br>Lys        | tct<br>Ser        | ttc<br>Phe         | tta<br>Leu<br>200 | gct<br>Ala        | att<br>lle        | cca<br>Pro        | aac<br>Asn        | tta<br>Leu<br>205 | 986  |
| gtt<br>Val        | att<br>lle        | ttt<br>Phe        | gca<br>Ala        | gtt<br>Val<br>210 | ttg<br>Leu        | tta<br>Leu        | ttt<br>Phe        | ttt<br>Phe        | tcc<br>Ser<br>215  | tca<br>Ser        | ttg<br>Leu        | gaa<br>Glu        | act<br>Thr        | ccc<br>Pro<br>220 | aaa<br>Lys        | 1034 |
| aat<br>Asn        | ccg<br>Pro        | att<br>He         | gct<br>Ala<br>225 | ttt<br>Phe        | Ala               | tgt<br>Cys        | Phe               | Phe               | Пe                 | Cys               | ctg<br>Leu        | Пe                | act<br>Thr<br>235 | Asp               | cct<br>Pro        | 1082 |
| ttc<br>Phe        | ctt<br>Leu        | gac<br>Asp<br>240 | att<br>lle        | tat<br>Tyr        | ttt<br>Phe        | agt<br>Ser        | gga<br>Gly<br>245 | ctt<br>Leu        | tca<br>Ser         | gta<br>Val        | act<br>Thr        | gaa<br>Glu<br>250 | aga<br>Arg        | tgg<br>Trp        | aaa<br>Lys        | 1130 |
| Pro               | ttt<br>Phe<br>255 | ttg<br>Leu        | tac<br>Tyr        | cgt<br>Arg        | gga<br>Gly        | aga<br>Arg<br>260 | att<br>He         | tgc<br>Cys        | aga<br>Arg         | aga<br>Arg        | ctt<br>Leu<br>265 | tca<br>Ser        | gtc<br>Val        | gtt<br>Val        | ttt<br>Phe        | 1178 |
| gct<br>Ala<br>270 | gga<br>Gly        | atg<br>Met        | att<br>He         | gag<br>Glu        | ctt<br>Leu<br>275 | aca<br>Thr        | ttt<br>Phe        | ttt<br>Phe        | att<br>lle         | ctt<br>Leu<br>280 | tcc<br>Ser        | gca<br>Ala        | ttc<br>Phe        | aaa<br>Lys        | ctt<br>Leu<br>285 | 1226 |
| aga<br>Arg        | gac<br>Asp        | act<br>Thr        | His               | ctc<br>Leu<br>290 | tgg<br>Trp        | tat<br>Tyr        | ttt<br>Phe        | Val               | ata<br>1 le<br>295 | cct<br>Pro        | ggc<br>Gly        | ttt<br>Phe        | tcc<br>Ser        | att<br>lle<br>300 | ttt<br>Phe        | 1274 |
| gga<br>Gly        | att<br>He         | ttc<br>Phe        | tgg<br>Trp        | atg<br>Met        | att<br>He         | tgt<br>Cys        | cat<br>His        | att<br>lle        | att<br>He          | ttt<br>Phe        | ctt<br>Leu        | tta<br>Leu        | act<br>Thr        | ctt<br>Leu        | tgg<br>Trp        | 1322 |



| gga<br>Gly            | ttc<br>Phe         | cat<br>His<br>320 | s in              | c aa<br>r Ly          | a ti<br>s Le       | a aa<br>eu As      | nt ga<br>n As<br>32 | зр Су                   | c ca<br>s Hi       | it aa<br>s Ly       | a gt<br>s Va       | a ta<br>  Ty<br>  33      | r Ph                         | t ac<br>ne Th        | t cac<br>r His        | 1370 |
|-----------------------|--------------------|-------------------|-------------------|-----------------------|--------------------|--------------------|---------------------|-------------------------|--------------------|---------------------|--------------------|---------------------------|------------------------------|----------------------|-----------------------|------|
| agg<br>Arg            | aca<br>Thr<br>335  | gat<br>Asp        | ta<br>Ty          | c aa<br>r As          | t ag<br>n Se       | c ct<br>r Le<br>34 | u As                | it ag<br>p Ar           | a at<br>g          | c at<br>e Me        | g gc<br>t Al<br>34 | a Se                      | c aa<br>r Ly                 | a gg<br>s Gl         | g atg<br>y Met        | 1418 |
| cgc<br>Arg<br>350     | cat<br>His         | ttt<br>Phe        | tge<br>Cys        | c ttg<br>s Lei        | g at<br>u 11<br>35 | e Se               | a ga<br>r Gl        | g ca<br>u Gi            | g tt<br>n Le       | g gt<br>u Va<br>360 | l Ph               | c tt <sup>.</sup><br>e Ph | t ag<br>e Se                 | t ct<br>r Le         | t ctt<br>u Leu<br>365 | 1466 |
| gca<br>Ala            | aca<br>Thr         | gcg<br>Ala        | ; att             | t ttg<br>e Lei<br>370 | ı Gi               | a gc<br>y Al       | a gt<br>a Va        | t to<br>  Se            | c tg<br>r Tr<br>37 | p Gli               | g cca<br>n Pro     | a aca<br>o Thi            | a aa<br>r As                 | t gg<br>n Gly<br>380 | a att<br>y lle<br>)   | 1514 |
| ttc<br>Phe            | ttg<br>Leu         | agc<br>Ser        | atg<br>Met<br>385 | $:$ Ph $\epsilon$     | ct<br>Le           | a ato<br>u lle     | c gt<br>e Va        | t tt:<br>  Le:<br>  390 | ı Pro              | a ttg<br>o Lei      | g gaa<br>u Glu     | a too<br>u Ser            | at;<br>Me <sup>-</sup><br>39 | t Ala                | t cat<br>a His        | 1562 |
| GIY                   | Leu                | 400               | HIS               | Glu                   | ı Lei              | u Gly              | / Asr<br>405        | n Cys                   | i Lei              | ı Gly               | / Gly              | / Thr<br>410              | Sei                          | <sup>r</sup> Val     | gga<br>Gly            | 1610 |
|                       | 415                | пе                | val               | ire                   | Pro                | 420                | Asr                 | ı Phe                   | : Cys              | Ser                 | Pro<br>425         | Asp                       | Gly                          | / Gir                | Pro                   | 1658 |
| aca d<br>Thr L<br>430 | _eu i              | Leu               | Pro               | Pro                   | 435                | l His              | Val                 | GIn                     | Glu                | Leu<br>440          | Asn                | Leu                       | Arg                          | Ser                  | Thr<br>445            | 1706 |
| ggc a<br>Gly M        | iet i              | _eu               | ASN               | 450                   | пе                 | GIN                | Arg                 | Phe                     | 455                | Ala                 | Tyr                | His                       | Met                          | 11e<br>460           | Glu                   | 1754 |
| acc t<br>Thr T        | yr (               | зіу               | 465               | Asp                   | lyr                | Ser                | Ihr                 | Ser<br>470              | Gly                | Leu                 | Ser                | Phe                       | Asp<br>475                   | Thr                  | Leu                   | 1802 |
| cat t<br>His S        | 4                  | 180               | Leu               | Lys                   | нιа                | Phe                | 485                 | Glu                     | Leu                | Arg                 | lhr                | Val<br>490                | Asp                          | Gly                  | Pro                   | 1850 |
| aga c<br>Arg H<br>4   | at g<br>is A<br>95 | at i              | acg<br>Thr        | tat<br>Tyr            | att<br>He          | ttg<br>Leu<br>500  | tat<br>Tyr          | tac<br>Tyr              | agt<br>Ser         | ggg<br>Gly          | cac<br>His<br>505  | acc<br>Thr                | cat<br>His                   | ggt<br>Gly           | aca<br>Thr            | 1898 |
| gga g<br>Gly G<br>510 | ag t<br>Iu T       | gg £<br>rp /      | gct<br>Ala        | Leu                   | gca<br>Ala<br>515  | ggt<br>Gly         | gga<br>Gly          | gat<br>Asp              | aca<br>Thr         | cta<br>Leu<br>520   | cgc<br>Arg         | ctt<br>Leu                | gac<br>Asp                   | aca<br>Thr           | ctt<br>Leu<br>525     | 1946 |
| ata ga<br>lle G       | aa t<br>Iu T       | gg t<br>rp T      | rp ,              | aga<br>Arg<br>530     | gaa<br>Glu         | aag<br>Lys         | aat<br>Asn          | Gly                     | tcc<br>Ser<br>535  | ttt<br>Phe          | tgt<br>Cys         | tcc<br>Ser                | cgg<br>Arg                   | ctt<br>Leu<br>540    | att<br>He             | 1994 |

| ato<br>lle        | gta<br>Val        | ı tta<br>Leu      | gac<br>Asp<br>545 | Ser               | a lu              | aat<br>Asn        | tca<br>Ser        | acc<br>Thr<br>550 | Pro               | tgg<br>Trp        | g gtg<br>Val      | aaa<br>Lys        | §<br>G ru<br>555  | gtg<br>Val        | agg<br>Arg        | 2042 |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| aaa<br>Lys        | att<br>lle        | aat<br>Asn<br>560 | gac<br>Asp        | cag<br>Gln        | tat<br>Tyr        | att               | gca<br>Ala<br>565 | gtg<br>Val        | caa<br>Gln        | gga<br>Gly        | gca<br>Ala        | gag<br>Glu<br>570 | ttg<br>Leu        | ata<br>Ile        | aaa<br>Lys        | 2090 |
| aca<br>Thr        | gta<br>Val<br>575 | gat<br>Asp        | att<br>lle        | gaa<br>Glu        | gaa<br>Glu        | gct<br>Ala<br>580 | gac<br>Asp        | ccg<br>Pro        | cca<br>Pro        | cag<br>Gln        | cta<br>Leu<br>585 | ggt<br>Gly        | gac<br>Asp        | ttt<br>Phe        | aca<br>Thr        | 2138 |
| aaa<br>Lys<br>590 | gac<br>Asp        | tgg<br>Trp        | gta<br>Val        | gaa<br>Glu        | tat<br>Tyr<br>595 | aac<br>Asn        | tgc<br>Cys        | aac<br>Asn        | tcc<br>Ser        | agt<br>Ser<br>600 | aat<br>Asn        | aac<br>Asn        | atc<br>lle        | tgc<br>Cys        | tgg<br>Trp<br>605 | 2186 |
| act<br>Thr        | gaa<br>Glu        | aag<br>Lys        | gga<br>Gly        | cgc<br>Arg<br>610 | aca<br>Thr        | gtg<br>Val        | aaa<br>Lys        | gca<br>Ala        | gta<br>Val<br>615 | tat<br>Tyr        | ggt<br>Gly        | gtg<br>Val        | tca<br>Ser        | aaa<br>Lys<br>620 | cgg<br>Arg        | 2234 |
| tgg<br>Trp        | agt<br>Ser        | gac<br>Asp        | tac<br>Tyr<br>625 | act<br>Thr        | ctg<br>Leu        | cat<br>His        | ttg<br>Leu        | cca<br>Pro<br>630 | acg<br>Thr        | gga<br>Gly        | agc<br>Ser        | gat<br>Asp        | gtg<br>Val<br>635 | gcc<br>Ala        | aag<br>Lys        | 2282 |
| cac<br>His        | tgg<br>Trp        | atg<br>Met<br>640 | tta<br>Leu        | cac<br>His        | ttt<br>Phe        | Pro               | cgt<br>Arg<br>645 | att<br>Ile        | aca<br>Thr        | tat<br>Tyr        | ccc<br>Pro        | cta<br>Leu<br>650 | gtg<br>Val        | cat<br>His        | ttg<br>Leu        | 2330 |
| Ara               | aat<br>Asn<br>655 | tgg<br>Trp        | tta<br>Leu        | tgc<br>Cys        | Gly               | ctg<br>Leu<br>660 | aac<br>Asn        | ctt<br>Leu        | ttt<br>Phe        | Trp               | atc<br>Ile<br>665 | tgc<br>Cys        | aaa<br>Lys        | act<br>Thr        | tgt<br>Cys        | 2378 |
| ttt<br>Phe<br>670 | agg<br>Arg        | tgc<br>Cys I      | ttg i<br>Leu l    | ∟ys               | aga<br>Arg<br>675 | tta<br>Leu l      | aaa<br>Lys        | atg<br>Met        | Ser               | tgg<br>Trp<br>680 | ttt<br>Phe        | ctt<br>Leu l      | cct<br>Pro        | Thr               | gtg<br>Val<br>685 | 2426 |
| ctg<br>Leu        | gac<br>Asp        | aca g<br>Thr (    | ily (             | caa<br>Gln<br>690 | ggc<br>Gly I      | ttc a<br>Phe l    | aaa (<br>_ys      | Leu '             | gtc<br>Val<br>695 | aaa<br>Lys        | tct<br>Ser        | taat <sup>.</sup> | ttgg              | ac                | ·                 | 2472 |
| ccca              | aagc              | gg ga             | atatt             | taat              | a ago             | cacto             | cata              | cta               | ccaa              | tta               | tcac              | taact             | tt go             | ccat              | ttttt             | 2532 |
| gtatį             | gctg              | ta tt             | ttta              | attt              | g tgg             | gaaaa             | atac              | ctt               | gcta              | ctt               | ctgta             | agcte             | gc to             | ctca              | ctttg             | 2592 |
| tctt              | ttct              | ta ag             | gtaat             | tat               | g gta             | atata             | ataa              | ggc               | gttg              | gga               | aaaa              | acatt             | tt ta             | ataa              | tgaaa             | 2652 |
| gtate             | gtag              | gg ag             | gtcaa             | atgo              | c tta             | actgt             | aaa               | tgca              | ataa              | gag               | acgt1             | taaaa             | aa ta             | acad              | ctgca             | 2712 |
| ctttc             | cagga             | aa tg             | tttg              | ctta              | a tgg             | tcct              | gat               | taga              | aaaga             | aaa d             | cagtt             | gtct              | a tg              | ctct              | gcaa              | 2772 |
| tggto             | aatg              | ga tg             | aatt              | acta              | a atg             | cctt              | att               | ttct              | aggo              | cat a             | ataat             | aata              | ıg tt             | taga              | agaat             | 2832 |
| gtaga             | ccag              | ga ta             | aatt              | tgtt              | tac               | tgtt              | tta               | agaa              | aact              | ac o              | cagtt             | tact              | t ac              | agaa              | gatt              | 2892 |
| ctttt             | ttcc              | a aa              | cagt              | aggt              | ttc               | atcc              | aag               | асса              | tttg              | gaa g             | gaact             | gcaa              | a ct              | cttt              | ctct              | 2952 |
| tagaa             | aaga              | a ag              | aggg              | cago              | cta               | aaat              | aaa               | cgca              | aaat              | tt g              | ctta              | tact              | с са              | tcac              | :                 | 3008 |

| <21<br><21<br><21<br><21 | 1> 6<br>2> P | 11<br>RT   | sapi       | ens        |            |            |            | 1          |            |            |            |            |            |            |            |
|--------------------------|--------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
|                          | 0> 7<br>Glu  |            | Ala        | Ser<br>5   | Leu        | Ser        | Leu        | Ser        | Asn<br>10  | Leu        | Trp        | Phe        | Gly        | Phe<br>15  | Leu        |
| Leu                      | Gly          | Leu        | Leu<br>20  | Cys        | Phe        | Leu        | Asp        | Asn<br>25  | Ser        | Ser        | Phe        | Lys        | Asn<br>30  | Asp        | Val        |
| Lys                      | Glu          | Glu<br>35  | Ser        | Thr        | Lys        | Tyr        | Leu<br>40  | Leu        | Leu        | Thr        | Ser        | lle<br>45  | Val        | Leu        | Arg        |
| lle                      | Leu<br>50    | Cys        | Ser        | Leu        | Val        | Glu<br>55  | Arg        | lle        | Ser        | Gly        | Tyr<br>60  | Val        | Arg        | His        | Arg        |
| Pro<br>65                | Thr          | Leu        | Leu        | Thr        | Thr<br>70  | Val        | Glu        | Phe        | Leu        | Glu<br>75  | Leu        | Val        | Gly        | Phe        | Ala<br>80  |
| lle                      | Ala          | Ser        | Thr        | Thr<br>85  | Met        | Leu        | Val        | Glu        | Lys<br>90  | Ser        | Leu        | Ser        | Val        | lle<br>95  | Leu        |
| Leu                      | Val          | Val        | Ala<br>100 | Leu        | Ala        | Met        | Leu        | lle<br>105 | He         | Asp        | Leu        | Arg        | Met<br>110 | Lys        | Ser        |
| Phe                      | Leu          | Ala<br>115 | lle        | Pro        | Asn        | Leu        | Val<br>120 | He         | Phe        | Ala        | Val        | Leu<br>125 | Leu        | Phe        | Phe        |
| Ser                      | Ser<br>130   | Leu        | Glu        | Jhr        | Pro        | Lys<br>135 | Asn        | Pro        | He         | Ala        | Phe<br>140 | Ala        | Cys        | Phe        | Phe        |
| 11e<br>145               | Cys          | Leu        | lle        | Thr        | Asp<br>150 | Pro        | Phe        | Leu        | Asp        | lle<br>155 | Tyr        | Phe        | Ser        | Gly        | Leu<br>160 |
| Ser                      | Val          | Thr        | Glu        | Arg<br>165 | Trp        | Lys        | Pro        | Phe        | Leu<br>170 | Tyr        | Arg        | Gly        | Arg        | lle<br>175 | Cys        |
| Arg                      | Arg          | Leu        | Ser<br>180 | Val        | Val        | Phe        | Ala        | Gly<br>185 | Met        | lle        | Glu        | Leu        | Thr<br>190 | Phe        | Phe        |
| lle                      | Leu          | Ser<br>195 | Ala        | Phe        | Lys        | Leu        | Arg<br>200 | Asp        | Thr        | His        | Leu        | Trp<br>205 | Tyr        | Phe        | Val        |
| lle                      | Pro<br>210   | Gly        | Phe        | Ser        | Пе         | Phe<br>215 | Gly        | He         | Phe        | Trp        | Met<br>220 | He         | Cys        | His        | He         |
| 11e<br>225               | Phe          | Leu        | Leu        | Thr        | Leu<br>230 | Trp        | Gly        | Phe        | His        | Thr<br>235 | Lys        | Leu        | Asn        | Asp        | Cys<br>240 |
| His                      | Lys          | Val        | Tyr        | Phe<br>245 | Thr        | His        | Arg        | Thr        | Asp<br>250 | Tyr        | Asn        | Ser        | Leu        | Asp<br>255 | Arg        |
| Пe                       | Met          | Ala        | Ser<br>260 | Lys        | Gly        | Met        | Arg        | His<br>265 | Phe        | Cys        | Leu        | He         | Ser<br>270 | Glu        | Gln        |

| Leu        | Val        | Phe<br>275 |            | Se <sub>1</sub> | <b>O</b> u | Leu        | 1 Ala<br>280 | Thr        | Ala        | ılle       | : Leu      | Gly<br>285 |            | Val        | Se         |
|------------|------------|------------|------------|-----------------|------------|------------|--------------|------------|------------|------------|------------|------------|------------|------------|------------|
| Trp        | GIn<br>290 | Pro        | Thr        | Asn             | Gly        | 11e<br>295 | Phe          | Leu        | Ser        | Met        | Phe<br>300 |            | lle        | Val        | Lei        |
| Pro<br>305 | Leu        | Glu        | Ser        | Met             | Ala<br>310 | His        | Gly          | Leu        | Phe        | His<br>315 |            | Leu        | Gly        | Asn        | Cys<br>320 |
| Leu        | Gly        | Gly        | Thr        | Ser<br>325      | Val        | Gly        | Tyr          | Ala        | lle<br>330 |            | lle        | Pro        | Thr        | Asn<br>335 | Phe        |
| Cys        | Ser        | Pro        | Asp<br>340 | Gly             | Gln        | Pro        | Thr          | Leu<br>345 |            | Pro        | Pro        | Glu        | His<br>350 | Val        | Glr        |
| Glu        | Leu        | Asn<br>355 | Leu        | Arg             | Ser        | Thr        | Gly<br>360   | Met        | Leu        | Asn        | Ala        | lle<br>365 | Gln        | Arg        | Phe        |
| Phe        | Ala<br>370 | Tyr        | His        | Met             | lle        | Glu<br>375 | Thr          | Tyr        | Gly        | Cys        | Asp<br>380 | Tyr        | Ser        | Thr        | Ser        |
| Gly<br>385 | Leu        | Ser        | Phe        | Asp             | Thr<br>390 | Leu        | His          | Ser        | Lys        | Leu<br>395 | Lys        | Ala        | Phe        | Leu        | G u        |
| Leu        | Arg        | Thr        | Val        | Asp<br>405      | Gly        | Pro        | Arg          | His        | Asp<br>410 | Thr        | Tyr        | lle        | Leu        | Tyr<br>415 | Tyr        |
| Ser        | Gly        | His        | Thr        | His             | Glv        | Thr        | Glv          | Glu        | Trn        | Ala        | Leu        | αا۵        | GLv        | GLv        | Aen        |

Ser Gly His Thr His Gly Thr Gly Glu Trp Ala Leu Ala Gly Gly Asp 420 430

Thr Leu Arg Leu Asp Thr Leu lie Glu Trp Trp Arg Glu Lys Asn Gly
435
440
445

Ser Phe Cys Ser Arg Leu IIe IIe Val Leu Asp Ser Glu Asn Ser Thr 450 455 460

Pro Trp Val Lys Glu Val Arg Lys IIe Asn Asp Gln Tyr IIe Ala Val 465 470 475 480

Gln Gly Ala Glu Leu Ile Lys Thr Val Asp Ile Glu Glu Ala Asp Pro 485 490 495

Pro Gln Leu Gly Asp Phe Thr Lys Asp Trp Val Glu Tyr Asn Cys Asn 500 510

Ser Ser Asn Asn Ile Cys Trp Thr Glu Lys Gly Arg Thr Val Lys Ala 515 520 525

Val Tyr Gly Val Ser Lys Arg Trp Ser Asp Tyr Thr Leu His Leu Pro 530 540

Thr Gly Ser Asp Val Ala Lys His Trp Met Leu His Phe Pro Arg Ile 545 550 555 560

Thr Tyr Pro Leu Val His Leu Ala Asn Trp Leu Cys Gly Leu Asn Leu 565 570 575

Phe Trp IIe Cys Lys Thr Cys Phe Arg Cys Leu Lys Arg Leu Lys Met

580

Ser Trp Phe Leu Pro Thr Val Leu Asp Thr Gly Gln Gly Phe Lys Leu

Val Lys Ser 610

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cgccagcata ctctattact attttca atg gaa gca gca agt tta agt ctc 652 Met Glu Ala Ala Ser Leu Ser Leu

tcc aat ctt tgg ttt gga ttc ttg ctt ggc ctc cta tgt ttt ctt gat 700 Ser Asn Leu Trp Phe Gly Phe Leu Leu Gly Leu Leu Cys Phe Leu Asp

aat tca tcc ttt aaa aat gat gta aaa gaa gaa tca acc aaa tat ttg 748 Asn Ser Ser Phe Lys Asn Asp Val Lys Glu Glu Ser Thr Lys Tyr Leu 25

ctt cta aca tcc ata gtg tta agg ata ttg tgc tct ctg gtg gag aga 796 Leu Leu Thr Ser lie Val Leu Arg lie Leu Cys Ser Leu Val Glu Arg 45

att tot ggt tat gtc cgt cat cgg ccc act tta cta acc aca gtt gaa lle Ser Gly Tyr Val Arg His Arg Pro Thr Leu Leu Thr Thr Val Glu 60

|        |                   |                   |                   |                   | - 1               |                   |                   |                   |                   |                   |                   |                   |                   |                   | A                 |                   |      |
|--------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
|        | ttt<br>Phe        | ctg<br>Leu        | gag<br>Glu<br>75  | Leu               | gtt<br>Val        | gga<br>Gly        | ttt<br>Phe        | gcc<br>Ala<br>80  | Пe                | gcc<br>Ala        | agc<br>Ser        | aca<br>Thr        | act<br>Thr<br>85  | Met               | ttg<br>Leu        | gtg<br>Val        | 892  |
|        | gag<br>Glu        | aag<br>Lys<br>90  | Ser               | ctg<br>Leu        | agt<br>Ser        | gtc<br>Val        | att<br>Ile<br>95  | Leu               | ctt<br>Leu        | gtt<br>Val        | gta<br>Val        | gct<br>Ala<br>100 | Leu               | gct<br>Ala        | atg<br>Met        | ctg<br>Leu        | 940  |
|        | att<br>He<br>105  | Пe                | gat<br>Asp        | ctg<br>Leu        | aga<br>Arg        | atg<br>Met<br>110 | Lys               | tct<br>Ser        | ttc<br>Phe        | tta<br>Leu        | gct<br>Ala<br>115 | He                | cca<br>Pro        | aac<br>Asn        | tta<br>Leu        | gtt<br>Val<br>120 | 988  |
|        | att<br>He         | ttt<br>Phe        | gca<br>Ala        | gtt<br>Val        | ttg<br>Leu<br>125 | Leu               | ttt<br>Phe        | ttt<br>Phe        | tcc<br>Ser        | tca<br>Ser<br>130 | Leu               | gaa<br>Glu        | act<br>Thr        | ccc<br>Pro        | aaa<br>Lys<br>135 | aat<br>Asn        | 1036 |
| İ      | ccg<br>Pro        | att<br>lle        | gct<br>Ala        | ttt<br>Phe<br>140 | gcg<br>Ala        | tgt<br>Cys        | ttt<br>Phe        | ttt<br>Phe        | att<br>IIe<br>145 | tgc<br>Cys        | ctg<br>Leu        | ata<br>Ile        | act<br>Thr        | gat<br>Asp<br>150 | cct<br>Pro        | ttc<br>Phe        | 1084 |
| i      | ctt<br>Leu        | gac<br>Asp        | att<br>Ile<br>155 | tat<br>Tyr        | ttt<br>Phe        | agt<br>Ser        | gga<br>Gly        | ctt<br>Leu<br>160 | tca<br>Ser        | gta<br>Val        | act<br>Thr        | gaa<br>Glu        | aga<br>Arg<br>165 | tgg<br>Trp        | aaa<br>Lys        | ccc<br>Pro        | 1132 |
| ı      | ttt<br>Phe        | ttg<br>Leu<br>170 | tac<br>Tyr        | cgt<br>Arg        | gga<br>Gly        | aga<br>Arg        | att<br>11e<br>175 | tgc<br>Cys        | aga<br>Arg        | aga<br>Arg        | ctt<br>Leu        | tca<br>Ser<br>180 | gtc<br>Val        | gtt<br>Val        | ttt<br>Phe        | gct<br>Ala        | 1180 |
| (      | gga<br>Gly<br>185 | atg<br>Met        | att<br>lle        | gag<br>Glu        | ctt<br>Leu<br>`   | aca<br>Thr<br>190 | ttt<br>Phe        | ttt<br>Phe        | att<br>He         | ctt<br>Leu        | tcc<br>Ser<br>195 | gca<br>Ala        | ttc<br>Phe        | aaa<br>Lys        | ctt<br>Leu        | aga<br>Arg<br>200 | 1228 |
| £      | gac<br>Asp        | act<br>Thr        | cac<br>His        | ctc<br>Leu        | tgg<br>Trp<br>205 | tat<br>Tyr        | ttt<br>Phe        | gta<br>Val        | ata<br>He         | cct<br>Pro<br>210 | ggc<br>Gly        | ttt<br>Phe        | tcc<br>Ser        | att<br>He         | ttt<br>Phe<br>215 | gga<br>Gly        | 1276 |
| į      | att<br>He         | ttc<br>Phe        | tgg<br>Trp        | atg<br>Met<br>220 | att<br>He         | tgt<br>Cys        | cat<br>His        | att<br>He         | att<br>Ile<br>225 | ttt<br>Phe        | ctt<br>Leu        | tta<br>Leu        | act<br>Thr        | ctt<br>Leu<br>230 | tgg<br>Trp        | gga<br>Gly        | 1324 |
| ţ      | tc<br>he          | cat<br>His        | acc<br>Thr<br>235 | aaa<br>Lys        | tta<br>Leu        | aat<br>Asn        | gac<br>Asp        | tgc<br>Cys<br>240 | cat<br>His        | aaa<br>Lys        | gta<br>Val        | tat<br>Tyr        | ttt<br>Phe<br>245 | act<br>Thr        | cac<br>His        | agg<br>Arg        | 1372 |
| ā      | aca<br>hr         | gat<br>Asp<br>250 | tac<br>Tyr        | aat<br>Asn        | agc<br>Ser        | ctt<br>Leu        | gat<br>Asp<br>255 | aga<br>Arg        | atc<br>lle        | atg<br>Met        | gca<br>Ala        | tcc<br>Ser<br>260 | aaa<br>Lys        | ggg<br>Gly        | atg<br>Met        | cgc<br>Arg        | 1420 |
| Н      | at<br>lis<br>165  | ttt<br>Phe        | tgc<br>Cys        | ttg<br>Leu        | att<br>He         | tca<br>Ser<br>270 | gag<br>Glu        | cag<br>Gln        | ttg<br>Leu        | gtg<br>Val        | ttc<br>Phe<br>275 | ttt<br>Phe        | agt<br>Ser        | ctt<br>Leu        | ctt<br>Leu        | gca<br>Ala<br>280 | 1468 |
| a<br>T | ica<br>hr         | gcg<br>Ala        | att<br>lle        | ttg<br>Leu        | gga<br>Gly<br>285 | gca<br>Ala        | gtt<br>Val        | tcc<br>Ser        | tgg<br>Trp        | cag<br>G n<br>290 | cca<br>Pro        | aca<br>Thr        | aat<br>Asn        | gga<br>Gly        | att<br>He<br>295  | ttc<br>Phe        | 1516 |
| t      | tg                | agc               | atg               | ttt               | cta               | atc               | gtt               | ttg               | сса               | ttg               | gaa               | tcc               | atg               | gct               | cat               | ggg               | 1564 |

| Leu               | Ser               | Met               | Phe               |                   |                   | Val               | Leu               |                   |                   | Glu               | Ser               | Met               | _                 |                   | Gly               |      |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| ctc               | ttc               | cat               | 300<br>gaa        |                   | øøt               | aac               | t øt              | 305<br>tta        |                   | σσα               | aca               | tet               | 310               | gga               | t at              | 1612 |
| Leu               | Phe               | His<br>315        | Glu               | Leu               | Gly               | Asn               | Cys<br>320        | Leu               | Gly               | Gly               | Thr               | Ser<br>325        | Val               | Gly               | Tyr               | 1012 |
| gct<br>Ala        | att<br>lle<br>330 | Val               | att<br>lle        | ccc<br>Pro        | acc<br>Thr        | aac<br>Asn<br>335 | ttc<br>Phe        | tgc<br>Cys        | agt<br>Ser        | cct<br>Pro        | gat<br>Asp<br>340 | Gly               | cag<br>Gln        | cca<br>Pro        | aca<br>Thr        | 1660 |
| ctg<br>Leu<br>345 | Leu               | ccc<br>Pro        | cca<br>Pro        | gaa<br>Glu        | cat<br>His<br>350 | gta<br>Val        | cag<br>Gln        | gag<br>Glu        | tta<br>Leu        | aat<br>Asn<br>355 | ttg<br>Leu        | agg<br>Arg        | tct<br>Ser        | act<br>Thr        | ggc<br>Gly<br>360 | 1708 |
|                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | gag<br>Glu<br>375 |                   | 1756 |
|                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | ctg<br>Leu        |                   | 1804 |
| tcc<br>Ser        | aaa<br>Lys        | cta<br>Leu<br>395 | aaa<br>Lys        | gct<br>Ala        | ttc<br>Phe        | ctc<br>Leu        | gaa<br>Glu<br>400 | ctt<br>Leu        | cgg<br>Arg        | aca<br>Thr        | gtg<br>Val        | gat<br>Asp<br>405 | gga<br>Gly        | ccc<br>Pro        | aga<br>Arg        | 1852 |
|                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | aca<br>Thr        |                   | 1900 |
|                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | ctt<br>Leu        |                   | 1948 |
|                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | att<br>Ile<br>455 |                   | 1996 |
| gta<br>Val        | tta<br>Leu        | gac<br>Asp        | agc<br>Ser<br>460 | gaa<br>G u        | aat<br>Asn        | tca<br>Ser        | acc<br>Thr        | cct<br>Pro<br>465 | tgg<br>Trp        | gtg<br>Val        | aaa<br>Lys        | gaa<br>Glu        | gtg<br>Val<br>470 | agg<br>Arg        | aaa<br>Lys        | 2044 |
| att<br>lle        | aat<br>Asn        | gac<br>Asp<br>475 | cag<br>Gln        | tat<br>Tyr        | att<br>He         | gca<br>Ala        | gtg<br>Val<br>480 | caa<br>G n        | gga<br>Gly        | gca<br>Ala        | gag<br>Glu        | ttg<br>Leu<br>485 | ata<br>He         | aaa<br>Lys        | aca<br>Thr        | 2092 |
|                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | aca<br>Thr        |                   | 2140 |
| gac<br>Asp<br>505 | tgg<br>Trp        | gta<br>Val        | gaa<br>Glu        | tat<br>Tyr        | aac<br>Asn<br>510 | tgc<br>Cys        | aac<br>Asn        | tcc<br>Ser        | agt<br>Ser        | aat<br>Asn<br>515 | aac<br>Asn        | atc<br>lle        | tgc<br>Cys        | tgg<br>Trp        | act<br>Thr<br>520 | 2188 |
| gaa<br>Glu        | aag<br>Lys        | gga<br>Gly        | cgc<br>Arg        | aca<br>Thr<br>525 | gtg<br>Val        | aaa<br>Lys        | gca<br>Ala        | gta<br>Val        | tat<br>Tyr<br>530 | ggt<br>Gly        | gtg<br>Val        | tca<br>Ser        | aaa<br>Lys        | cgg<br>Arg<br>535 | tgg<br>Trp        | 2236 |

2284 agt gac tac act ctg at ttg cca acg gga agc gat gtg gas aag cac Ser Asp Tyr Thr Leu His Leu Pro Thr Gly Ser Asp Val Ala Lys His 540 tgg atg tta cac ttt cct cgt att aca tat ccc cta gtg cat ttg gca 2332 Trp Met Leu His Phe Pro Arg Ile Thr Tyr Pro Leu Val His Leu Ala 560 aat tgg tta tgc ggt ctg aac ctt ttt tgg atc tgc aaa act tgt ttt 2380 Asn Trp Leu Cys Gly Leu Asn Leu Phe Trp lle Cys Lys Thr Cys Phe 575 agg tgc ttg aaa aga tta aaa atg agt tgg ttt ctt cct act gtg ctg 2428 Arg Cys Leu Lys Arg Leu Lys Met Ser Trp Phe Leu Pro Thr Val Leu 590 595 gac aca gga caa ggc ttc aaa ctt gtc aaa tct taatttggac cccaaagcgg 2481 Asp Thr Gly Gln Gly Phe Lys Leu Val Lys Ser gatattaata agcactcata ctaccaatta tcactaactt gccatttttt gtatgctgta 2541 tttttatttg tggaaaatac cttgctactt ctgtagctgc tctcactttg tctttctta 2601 agtaattatg gtatatataa ggcgttggga aaaaacattt tataatgaaa gtatgtaggg 2661 agtcaaatgc ttactgtaaa tgcataagag acgttaaaaa taacactgca ctttcaggaa 2721 tgtttgctta tggtcctgat tagaaagaaa cagttgtcta tgctctgcaa tggtcaatga 2781 tgaattacta atgccttatt ttctaggcat ataataatag tttagagaat gtagaccaga 2841 taaatttgtt tactgtttta agaaaactac cagtttactt acagaagatt cttttttcca 2901 aacagtaggt ttcatccaag accatttgaa gaactgcaaa ctctttctct tagaaaagaa 2961 3007 agagggcagc ctaaaataaa cgcaaaattt gcttatactc catcac

<210> 81

<211> 184

<212> PRT

<213> Homo sapiens

<400> 81

Met Thr Ser Phe Glu Asp Ala Asp Thr Glu Glu Thr Val Thr Cys Leu
1 5 10 15

Gln Met Thr Val Tyr His Pro Gly Gln Leu Gln Cys Gly 11e Phe Gln 20 25 30

Ser lie Ser Phe Asn Arg Glu Lys Leu Pro Ser Ser Glu Val Lys 35 40 45

Phe Gly Arg Asn Ser Asn Ile Cys His Tyr Thr Phe Gln Asp Lys Gln 50 55 60

| Val<br>65                    | Ser            | Arg                | Val        | GI               | e<br>70          | Ser        | Leu        | Gln        | Leu             | Phe<br>75        | Lys        | Lys        |            | Asn              | Ser<br>80        |     |
|------------------------------|----------------|--------------------|------------|------------------|------------------|------------|------------|------------|-----------------|------------------|------------|------------|------------|------------------|------------------|-----|
| Ser                          | Val            | Leu                | Ser        | Phe<br>85        | Glu              | He         | Lys        | Asn        | Met<br>90       | Ser              | Lys        | Lys        | Thr        | Asn<br>95        | Leu              |     |
| lle                          | Val            | Asp                | Ser<br>100 | Arg              | Glu              | Leu        | Gly        | Tyr<br>105 | Leu             | Asn              | Lys        | Met        | Asp<br>110 | Leu              | Pro              |     |
| Tyr                          | Arg            | Cys<br>115         | Met        | Val              | Arg              | Phe        | Gly<br>120 | Glu        | Tyr             | Gln              | Phe        | Leu<br>125 | Met        | Glu              | Lys              |     |
| Glu                          | Asp<br>130     | Gly                | Glu        | Ser              | Leu              | G u<br>135 | Phe        | Phe        | Glu             | Thr              | Gln<br>140 | Phe        | He         | Leu              | Ser              |     |
| Pro<br>145                   | Arg            | Ser                | Leu        | Leu              | GIn<br>150       | Glu        | Asn        | Asn        | Trp             | Pro<br>155       | Pro        | His        | Arg        | Pro              | lle<br>160       |     |
| Pro                          | Glu            | Tyr                | Gly        | Thr<br>165       | Tyr              | Ser        | Leu        | Cys        | Ser<br>170      | Ser              | Gln        | Ser        | Ser        | Ser<br>175       | Pro              |     |
| Thr                          | Glu            | Met                | Asp<br>180 | Glu              | Asn              | Glu        | Ser        |            |                 |                  |            |            |            |                  |                  |     |
| <213<br><213<br><213<br><220 | )><br> > C[    | 617<br>NA<br>omo s |            |                  |                  |            |            |            |                 |                  |            |            |            |                  |                  |     |
|                              | )> 82<br>ttaca |                    | ggcc       | ccgg             | gc go            | cgaga      | aggao      | c gtg      | goto            | gcc              | agco       | cagte      | ggg a      | aaggo            | caggcc           | 60  |
| gcgc                         | cgcgc          | cgg g              | gagc       | gcgg             | ga gg            | gatc       | ggcg       | g cto      | cgcga           | gtca             | ctgg       | gtcc       | etg g      | gctcg            | ggttcc           | 120 |
| ccg                          | cacco          | ccg g              | gggc       | tcaca            | ac ti            | tacco      | cgcgc      | c gga      | aggag           | gcag             | cgg        | ccggg      | gtg 1      | tccad            | сссса            | 180 |
| tcct                         | tgcgo          | ccc a              | agtc       | tcct             | cg at            | ttcc       | cctc       | g cto      | ctgag           | gccg             | gga        | gagco      | ga a       | acago            | ctgaag           | 240 |
| agaį                         | gttca          | act g              | gacto      | ccca             | ag co            | ccca       | ggtgg      | g gco      | cttg            | tgca             | cato       |            | Th         |                  | t ttt<br>r Phe   | 296 |
| gaa<br>Glu<br>5              | gat<br>Asp     | gct<br>Ala         | gac<br>Asp | aca<br>Thr       | gaa<br>Glu<br>10 | gag<br>Glu | aca<br>Thr | gta<br>Val | act<br>Thr      | tgt<br>Cys<br>15 | ctc<br>Leu | cag<br>Gln | atg<br>Met | acg<br>Thr       | gtt<br>Val<br>20 | 344 |
| tac<br>Tyr                   | cat<br>His     | cct<br>Pro         | ggc<br>Gly | cag<br>Gln<br>25 | ttg<br>Leu       | cag<br>Gln | tgt<br>Cys | gga<br>Gly | ata<br>He<br>30 | ttt<br>Phe       | cag<br>Gln | tca<br>Ser | ata<br>Ile | agt<br>Ser<br>35 | ttt<br>Phe       | 392 |
|                              |                |                    |            |                  |                  |            |            |            | gtg<br>Val      |                  |            |            |            |                  |                  | 440 |

| tcc aac atc<br>Ser Asn Ile<br>55  | tgt cat t<br>Cys His T        | at act<br>yr Thr        | ttt cag<br>Phe Gln<br>60  | gac aaa<br>Asp Lys        | cag gtt<br>Gln Val<br>65  | tcc cga<br>Ser Arg            | gtt<br>Val            | 488   |
|-----------------------------------|-------------------------------|-------------------------|---------------------------|---------------------------|---------------------------|-------------------------------|-----------------------|-------|
| cag ttt tct<br>Gln Phe Ser<br>70  | ctg cag c<br>Leu Gln L        | tg ttt<br>eu Phe<br>75  | aaa aaa<br>Lys Lys        | ttc aac<br>Phe Asn        | agc tca<br>Ser Ser<br>80  | gtt cto<br>Val Leo            | tcc<br>Ser            | 536   |
| ttt gaa ata<br>Phe Glu lle<br>85  | aaa aat a<br>Lys Asn M        | tg agt<br>let Ser<br>90 | aaa aag<br>Lys Lys        | acc aat<br>Thr Asn<br>95  | ctg atc<br>Leu IIe        | gtg gad<br>Val Asp            | agc<br>Ser<br>100     | 584   |
| aga gag ctg<br>Arg Glu Leu        | ggc tac c<br>Gly Tyr L<br>105 | ta aat<br>.eu Asn       | aaa atg<br>Lys Met        | gac ctg<br>Asp Leu<br>110 | cca tac<br>Pro Tyr        | agg tgo<br>Arg Cys<br>115     | Met                   | 632   |
| gtc aga ttc<br>Val Arg Phe        | gga gag t<br>Gly Glu T<br>120 | at cag<br>yr Gln        | ttt ctg<br>Phe Leu<br>125 | atg gag<br>Met Glu        | aag gaa<br>Lys Glu        | gat ggd<br>Asp Gly<br>130     | gag<br>Glu            | 680   |
| tca ttg gaa<br>Ser Leu Glu<br>135 | ttt ttt g<br>Phe Phe G        | gag act<br>Hu Thr       | caa ttt<br>Gln Phe<br>140 | att tta<br>Ile Leu        | tct cca<br>Ser Pro<br>145 | aga toa<br>Arg Se             | a ctc<br>Leu          | 728   |
| ttg caa gaa<br>Leu Gin Giu<br>150 | aac aac t<br>Asn Asn 1        | gg cca<br>rp Pro<br>155 | cca cac<br>Pro His        | agg ccc<br>Arg Pro        | ata ccg<br>lle Pro<br>160 | gag ta<br>Glu Ty              | ggc<br>Gly            | 776   |
| act tat tcg<br>Thr Tyr Ser<br>165 | Leu Cys S                     | cc tcc<br>Ser Ser<br>70 | caa agc<br>Gln Ser        | agt tct<br>Ser Ser<br>175 | ccg aca<br>Pro Thr        | gaa at <sub>i</sub><br>Glu Me | g gat<br>E Asp<br>180 | 824 . |
| gaa aat gag<br>Glu Asn Glu        |                               | acaga a                 | aagtotaa                  | ga ggaga                  | aatat ga                  | tggatga                       | a                     | 876   |
| gagctctgta                        | gatgctgtat                    | agacad                  | ctaaa ta                  | agagttga                  | ttagggt                   | agt ata                       | tatagt                | 936   |
| catctgttat                        | gctgtgaaat                    | ttggaa                  | attca gt                  | attatcat                  | tttgaag                   | tct gta                       | aattgtg               | 996   |
| ttagtcatta                        | acttagtcac                    | ctgtt                   | gtatt ct                  | ggatctac                  | acaaaat                   | tat ttt                       | aactgct               | 1056  |
| cttattaatc                        | tgtgaggatt                    | aatata                  | acaaa aa                  | gtatcctt                  | tgagatg                   | aag tcg                       | tgttctc               | 1116  |
| aaaataaggt                        | tatattatt1                    | tcttt                   | ttctg ct                  | tgattttc                  | atcttgt                   | gtt ttg                       | ctttgtt               | 1176  |
| tttgtaagga                        | accatctct                     | ggttt                   | ggtca ca                  | tcagttca                  | caacagc                   | cat ttg                       | ttttcaa               | 1236  |
| ggtcaaggct                        | ccaggcagg                     | tgtta                   | ctggt gt                  | ttgcagcc                  | tgtcagt                   | act tgc                       | agtactg               | 1296  |
| gaataggttc                        | taggctagtø                    | g totgo                 | gcgtc ac                  | tgtggttt                  | tagcatg                   | gga gga                       | cttattt               | 1356  |
| gagaaatact                        | accttactt                     | tctat                   | gattt ct                  | ttttacag                  | agttata                   | gtg tgt                       | ttactcc               | 1416  |
| taagatgaca                        | gttctctttg                    | g totata                | attca gc                  | atctaaga                  | caaatat                   | tta aac                       | attttaa               | 1476  |
| agaaccactg                        | tgttaagtt                     | t aggat                 | tattt ac                  | ttaccaaa                  | ttagaag                   | ttt gac                       | ttttatg               | 1536  |

<210> 83

<211> 392

<212> PRT

<213> Homo sapiens

<400> 83

Met Asp Ala Arg Trp Trp Ala Val Val Leu Ala Ala Phe Pro Ser

Leu Gly Ala Gly Gly Glu Thr Pro Glu Ala Pro Pro Glu Ser Trp Thr

Gln Leu Trp Phe Phe Arg Phe Val Val Asn Ala Ala Gly Tyr Ala Ser

Phe Met Val Pro Gly Tyr Leu Leu Val Gln Tyr Phe Arg Arg Lys Asn

Tyr Leu Glu Thr Gly Arg Gly Leu Cys Phe Pro Leu Val Lys Ala Cys

Val Phe Gly Asn Glu Pro Lys Ala Ser Asp Glu Val Pro Leu Ala Pro

Arg Thr Glu Ala Ala Glu Thr Thr Pro Met Trp Gln Ala Leu Lys Leu 100

Leu Phe Cys Ala Thr Gly Leu Gln Val Ser Tyr Leu Thr Trp Gly Val

Leu Gin Glu Arg Val Met Thr Arg Ser Tyr Gly Ala Thr Ala Thr Ser

Pro Gly Glu Arg Phe Thr Asp Ser Gln Phe Leu Vai Leu Met Asn Arg

Val Leu Ala Leu Ile Val Ala Gly Leu Ser Cys Val Leu Cys Lys Gln

Pro Arg His Gly Ala Pro Met Tyr Arg Tyr Ser Phe Ala Ser Leu Ser 185

Asn Val Leu Ser Ser Trp Cys Gln Tyr Glu Ala Leu Lys Phe Val Ser

Phe Pro Thr Gln Val Leu Ala Lys Ala Ser Lys Val Ile Pro Val Met 215

Leu Met Gly Lys Leu Val Ser Arg Arg Ser Tyr Glu His Trp Glu Tyr 240

Leu Thr Ala Thr Leu Ile Ser Ile Gly Val Ser Met Phe Leu Leu Ser 245 250 255

| Ser Gly Pro Glu Pro Arg Ser Ser Pro Ala Thr Thr Leu Ser Gly Leu 260 265 270  |
|--|
| Phe Thr Val Gly Ser Leu Leu Glu Gln Gly Ala Leu Leu Glu Gly Thr<br>275 280 285   |
| Arg Phe Met Gly Arg His Ser Glu Phe Ala Ala His Ala Leu Leu Leu<br>290 295 300   |
| Ser lle Cys Ser Ala Cys Gly Gln Leu Phe Ile Phe Tyr Thr lle Gly<br>305 310 315 320   |
| Gin Phe Giy Ala Ala Vai Phe Thr Ile Ile Met Thr Leu Arg Gin Ala<br>325 330 335   |
| Phe Ala IIe Leu Leu Ser Cys Leu Leu Tyr Gly His Thr Val Thr Val<br>340 - 345 350   |
| Val Gly Gly Leu Gly Val Ala Val Phe Ala Ala Leu Leu Leu Arg<br>355 360 365   |
| Val Tyr Ala Arg Gly Arg Leu Lys Gin Arg Gly Lys Lys Ala Val Pro<br>370 375 380   |
| Val Glu Ser Pro Val Gln Lys Val<br>385 390   |
| <210> 84<br><211> 1898<br><212> DNA<br><213> Homo sapiens  |
| <220><br><221> CDS<br><222> (119) (1294)   |
| <400> 84 acttccgctg gccgctggct cgctggccgc tcctggaggc ggcggcggga gcgcaggggg 60  |
| cgcgcggccc ggggactcgc attccccggt tccccctcca ccccacgcgg cctggacc 118  |
| atg gac gcc aga tgg tgg gca gtg gtg gtg ctg gct gcg ttc ccc tcc 166<br>Met Asp Ala Arg Trp Trp Ala Val Val Leu Ala Ala Phe Pro Ser<br>1 5 10       |
| cta ggg gca ggt ggg gag act ccc gaa gcc cct ccg gag tca tgg acc 214<br>Leu Gly Ala Gly Gly Glu Thr Pro Glu Ala Pro Pro Glu Ser Trp Thr<br>20 25 30 |
| cag cta tgg ttc ttc cga ttt gtg gtg aat gct gct ggc tat gcc agc 262<br>Gln Leu Trp Phe Phe Arg Phe Val Val Asn Ala Ala Gly Tyr Ala Ser<br>35 40 45 |
| ttt atg gta cct ggc tac ctc ctg gtg cag tac ttc agg cgg aag aac 310 Phe Met Val Pro Gly Tyr Leu Leu Val Gln Tyr Phe Arg Arg Lys Asn 50 55 60       |

| tac ctg gag acc ggt gg ggc ctc tgc ttt ccc ctg gtg acc gct tgt 358 Tyr Leu Glu Thr Gly Arg Gly Leu Cys Phe Pro Leu Val Lys Ala Cys 65 70 75 80        |
|---|
| gtg ttt ggc aat gag ccc aag gcc tct gat gag gtt ccc ctg gcg ccc 406<br>Vai Phe Gly Asn Glu Pro Lys Ala Ser Asp Glu Vai Pro Leu Ala Pro<br>85 90 95    |
| cga aca gag gcg gca gag acc acc ccg atg tgg cag gcc ctg aag ctg 454<br>Arg Thr Glu Ala Ala Glu Thr Thr Pro Met Trp Gln Ala Leu Lys Leu<br>100 105 110 |
| ctc ttc tgt gcc aca ggg ctc cag gtg tct tat ctg act tgg ggt gtg 502<br>Leu Phe Cys Ala Thr Gly Leu Gln Val Ser Tyr Leu Thr Trp Gly Val<br>115 120 125 |
| ctg cag gaa aga gtg atg acc cgc agc tat ggg gcc aca gcc aca tca 550<br>Leu Gln Glu Arg Val Met Thr Arg Ser Tyr Gly Ala Thr Ala Thr Ser<br>130 135 140 |
| ccg ggt gag cgc ttt acg gac tcg cag ttc ctg gtg cta atg aac cga 598<br>Pro Gly Glu Arg Phe Thr Asp Ser Gln Phe Leu Val Leu Met Asn Arg<br>150 155 160 |
| gtg ctg gca ctg att gtg gct ggc ctc tcc tgt gtt ctc tgc aag cag 646<br>Val Leu Ala Leu Ile Val Ala Gly Leu Ser Cys Val Leu Cys Lys Gln<br>165 170 175 |
| ccc cgg cat ggg gca ccc atg tac cgg tac tcc ttt gcc agc ctg tcc 694<br>Pro Arg His Gly Ala Pro Met Tyr Arg Tyr Ser Phe Ala Ser Leu Ser<br>180 185     |
| aat gtg ctt agc agc tgg tgc caa tac gaa gct ctt aag ttc gtc agc 742<br>Asn Val Leu Ser Ser Trp Cys Gln Tyr Glu Ala Leu Lys Phe Val Ser<br>195 200 205 |
| ttc ccc acc cag gtg ctg gcc aag gcc tct aag gtg atc cct gtc atg 790<br>Phe Pro Thr Gin Val Leu Ala Lys Ala Ser Lys Val IIe Pro Val Met<br>210 215 220 |
| ctg atg gga aag ctt gtg tct cgg cgc agc tac gaa cac tgg gag tac 838<br>Leu Met Gly Lys Leu Val Ser Arg Arg Ser Tyr Glu His Trp Glu Tyr<br>230 235 240 |
| ctg aca gcc acc ctc atc tcc att ggg gtc agc atg ttt ctg cta tcc 886<br>Leu Thr Ala Thr Leu lle Ser lle Gly Val Ser Met Phe Leu Leu Ser<br>245 250 255 |
| agc gga cca gag ccc cgc agc tcc cca gcc acc aca ctc tca ggc ctc 934<br>Ser Gly Pro Glu Pro Arg Ser Ser Pro Ala Thr Thr Leu Ser Gly Leu<br>260 265 270 |
| ttc aca gtg ggc tca ctg cta gaa cag ggg gcc cta ctg gag gga acc 982<br>Phe Thr Val Gly Ser Leu Leu Glu Gly Ala Leu Leu Glu Gly Thr<br>275 280 285     |
| cgc ttc atg ggg cga cac agt gag ttt gct gcc cat gcc ctg cta ctc 1030  |

Arg Phe Met Gly Ar s Ser Glu Phe Ala Ala His Ala I tcc atc tgc tcc gca tgt ggc cag ctc ttc atc ttt tac acc att ggg 1078 Ser lle Cys Ser Ala Cys Gly Gln Leu Phe lle Phe Tyr Thr lle Gly cag ttt ggg gct gcc gtc ttc acc atc atc atg acc ctc cgc cag gcc 1126 Gin Phe Gly Ala Ala Val Phe Thr lie lie Met Thr Leu Arg Gin Ala 330 ttt gcc atc ctt ctc tgc ctt ctc tat ggc cac act gtc act gtg 1174 Phe Ala IIe Leu Leu Ser Cys Leu Leu Tyr Gly His Thr Val Thr Val 340 345 350 1222 Val Gly Gly Leu Gly Val Ala Val Val Phe Ala Ala Leu Leu Leu Arg 360 gtc tac gcg cgg ggc cgt cta aag caa cgg gga aag aag gct gtg cct 1270 Val Tyr Ala Arg Gly Arg Leu Lys Gln Arg Gly Lys Lys Ala Val Pro 380 gtt gag tct cct gtg cag aag gtt tgagggtgga aagggcctga ggggtgaagt Val Glu Ser Pro Val Gln Lys Val 385 390 gaaataggac cctcccacca tccccttctg ctgtaacctc tgagggagct ggctgaaagg 1384 gcaaaatgca ggtgttttct cagtatcaca gaccagctct gcagcagggg attggggagc 1444 ccaggaggca gccttccctt ttgccttaag tcacccatct tccagtaagc agtttattct 1504 gagccccggg ggtagacagt cctcagtgag gggttttggg gagtttgggg tcaagagagc 1564 ataggtaggt tccacagtta ctcttcccac aagttccctt aagtcttgcc ctagctgtgc 1624 tetgecacet tecagaetea eteceetetg caaataeetg catttettae eetggtgaga 1684 aaagcacaag cggtgtaggc tccaatgctg ctttcccagg agggtgaaga tggtgctgtg 1744 ctgaggaaag gggatgcaga gccctgccca gcaccaccac ctcctatgct cctggatccc 1804 taggctctgt tccatgagcc tgttgcaggt tttggtactt tagaaatgta actttttgct 1864 cttataattt tatttatta aattaaatta ctgc 1898

<210> 85

<211> 432

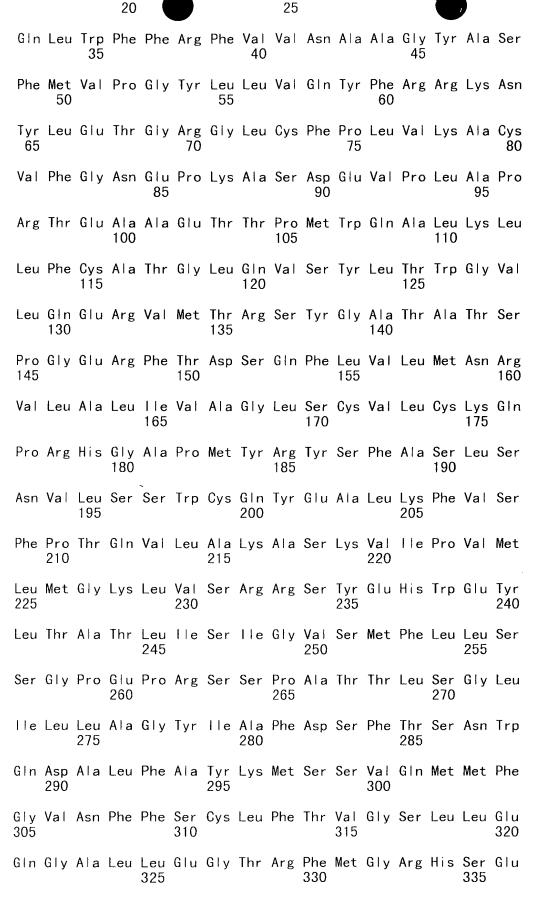
<212> PRT

<213> Homo sapiens

<400> 85

Met Asp Ala Arg Trp Trp Ala Val Val Leu Ala Ala Phe Pro Ser 1 5 10 15

Leu Gly Ala Gly Gly Glu Thr Pro Glu Ala Pro Pro Glu Ser Trp Thr



| Phe  | Ala   | Ala                                       | His<br>340  | Ala   | ∟eu  | Leu  | Leu  | Ser<br>345   | He   | Cys  | Ser   | Ala  | Cys<br>350   | Gly   | Gln  |   |
|--|---|---|---|---|--|--|--|--|--|--|---|--|--|---|--|---|
| Leu  | Phe   | lle<br>355                                | Phe   | Tyr   | Thr  | He   | Gly<br>360   | Gln  | Phe  | Gly  | Ala   | Ala<br>365   | Val  | Phe   | Thr  |   |
| He   | lle<br>370  | Met                                       | Thr   | Leu   | Arg  | Gln<br>375   | Ala  | Phe  | Ala  | lle  | Leu<br>380  | Leu  | Ser  | Cys   | Leu  |   |
| Leu<br>385   | Tyr   | Gly                                       | His   | Thr   | Val<br>390   | Thr  | Val  | Val  | Gly  | Gly<br>395   | Leu   | Gly  | Val  | Ala   | Val<br>400   |   |
| Val  | Phe   | Ala                                       | Ala   | Leu<br>405                                  | Leu  | Leu  | Arg  | Val  | Tyr<br>410   | Ala  | Arg   | Gly  | Arg  | Leu<br>415  | Lys  |   |
| Gln  | Arg   | Gly                                       | Lys<br>420  |   | Ala  | Val  | Pro  | Val<br>425   | Glu  | Ser  | Pro   | Val  | GIn<br>430   | Lys   | Val  |   |
| <21<br><21   | <210> 86<br><211> 2018<br><212> DNA<br><213> Homo sapiens |   |   |   |  |  |  |  |  |  |   |  |  |   |  |   |
| <220> <221> CDS <222> (119) (1414)   |   |   |   |   |  |  |  |  |  |  |   |  |  |   |  |   |
| <400> 86 acttccgctg gccgctggct cgctggccgc tcctggaggc ggcggcggga gcgcaggggg |   |   |   |   |  |  |  |  |  |  |   |  |  |   |  |   |
|  |   |   | gccgo   | ctggo                                       | ct c   | gctg   | gccgo  | c to   | ctgga  | aggc   | ggcį  | ggcgį  | gga į  | gcgca   | aggggg   | 60  |
| act <sup>-</sup>   |   | ctg g                                     |   | `   |  |  |  |  |  |  |   |  |  |   |  | 60<br>118   |
| act cgc;   | tccg  | ctg g<br>ccc g                            | gggga<br>aga  | ctcg<br>tgg                                 | gc at  | ttcco  | ccggt<br>gtg   | t tco  | cccc <sup>t</sup><br>gtg                                   | tcca<br>ctg  | ccc   | cacgo<br>gcg   | cgg (  | cctgg<br>ccc  | gacc<br>tcc  |   |
| actroggg<br>atg<br>Met<br>1  | tccgo<br>gcggo<br>gac                                     | ctg gcc gcc Ala                           | gggga<br>aga<br>Arg   | tgg<br>Trp<br>5                             | gc at<br>tgg<br>Trp<br>gag                           | gca<br>Ala<br>act  | gtg<br>Val   | gtg<br>Val<br>gaa  | gtg<br>Val<br>10   | ctg<br>Leu<br>cct                                    | gct<br>Ala  | gcg<br>Ala<br>gag                                    | ttc<br>Phe   | cctgg<br>ccc<br>Pro<br>15   | tcc<br>Ser<br>acc                                    | 118   |
| actrogcg<br>atg<br>Met<br>1<br>cta<br>Leu                                  | gegge<br>gac<br>Asp                                       | ctg gcc gcc Ala gca Ala                   | aga<br>Arg<br>ggt<br>Gly<br>20                                | tgg<br>Trp<br>5<br>ggg<br>Gly               | tgg<br>Trp<br>gag<br>Glu<br>cga                      | gca<br>Ala<br>act<br>Thr                                   | gtg<br>Val<br>ccc<br>Pro                                   | gtg<br>Val<br>gaa<br>Glu<br>25                             | gtg<br>Val<br>10<br>gcc<br>Ala                             | ctg<br>Leu<br>cct<br>Pro                             | gct<br>Ala<br>ccg<br>Pro  | gcg<br>Ala<br>gag<br>Glu                             | ttc<br>Phe<br>tca<br>Ser<br>30                             | ccc<br>Pro<br>15<br>tgg<br>Trp                                      | tcc<br>Ser<br>acc<br>Thr                             | 118<br>166  |
| actrong at g Met 1 cta Leu cag Gln   | gcggo<br>gac<br>Asp<br>ggg<br>Gly                         | ctg gcc gcc Ala gca Ala tgg Trp 35 gta    | aga<br>Arg<br>ggt<br>Gly<br>20<br>ttc<br>Phe                  | tgg<br>Trp<br>5<br>ggg<br>Gly<br>ttc<br>Phe | tgg<br>Trp<br>gag<br>Glu<br>cga<br>Arg               | gca<br>Ala<br>act<br>Thr<br>ttt<br>Phe                     | gtg<br>Val<br>ccc<br>Pro<br>gtg<br>Val<br>40               | gtg<br>Val<br>gaa<br>Glu<br>25<br>gtg<br>Val               | gtg<br>Val<br>10<br>gcc<br>Ala<br>aat<br>Asn               | ctg<br>Leu<br>cct<br>Pro<br>gct<br>Ala               | cccc<br>gct<br>Ala<br>ccg<br>Pro<br>gct<br>Ala                            | gcg<br>Ala<br>gag<br>Glu<br>ggc<br>Gly<br>45         | ttc<br>Phe<br>tca<br>Ser<br>30<br>tat<br>Tyr               | cctgg<br>ccc<br>Pro<br>15<br>tgg<br>Trp<br>gcc<br>Ala               | tcc<br>Ser<br>acc<br>Thr<br>agc<br>Ser               | 118<br>166<br>214   |
| actroggrammetric cgcs at g Met 1 cta Leu cag Gln ttt Phe tac               | gcggo<br>gac<br>Asp<br>ggg<br>Gly<br>cta<br>Leu<br>atg    | ctg gcc gcc Ala gca Ala tgg Trp5 gtal gag | agagga<br>aga<br>Arg<br>ggt<br>Gly<br>20<br>ttc<br>Phe<br>cct | tgg<br>Trp 5<br>ggg<br>Gly<br>ttc<br>Phe    | tgg<br>Trp<br>gag<br>Glu<br>cga<br>Arg<br>tac<br>Tyr | gca<br>Ala<br>act<br>Thr<br>ttt<br>Phe<br>ctc<br>Leu<br>55 | gtg<br>Val<br>ccc<br>Pro<br>gtg<br>Val<br>40<br>ctg<br>Leu | gtg<br>Va!<br>gaa<br>Glu<br>25<br>gtg<br>Va!<br>gtg<br>Va! | gtg<br>Val<br>10<br>gcc<br>Ala<br>aat<br>Asn<br>cag<br>Gln | ctg<br>Leu<br>cct<br>Pro<br>gct<br>Ala<br>tac<br>Tyr | cccc<br>gct<br>Ala<br>ccg<br>Pro<br>gct<br>Ala<br>ttc<br>Phe<br>60<br>ctg | gcg<br>Ala<br>gag<br>Glu<br>ggcy<br>45<br>agg<br>Arg | ttc<br>Phe<br>tca<br>Ser<br>30<br>tat<br>Tyr<br>cgg<br>Arg | cctgg<br>ccc<br>Pro<br>15<br>tgg<br>Trp<br>gcc<br>Ala<br>aag<br>Lys | tcc<br>Ser<br>acc<br>Thr<br>agc<br>Ser<br>aac<br>Asn | <ul><li>118</li><li>166</li><li>214</li><li>262</li></ul> |

| cga<br>Arg        | ac <i>a</i><br>Thr | gag<br>Glu        | gcg<br>Ala<br>100 | ı Ala             | g                 | acc<br>Thr        | acc<br>Thr        | ccg<br>Pro<br>105 | Met               | tgg<br>Trp        | cag<br>Gln        | gcc<br>Ala        | Leu<br>110        | Lys               | ctg<br>Leu        | 454  |
|-------------------|--------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| ctc<br>Leu        | ttc<br>Phe         | tgt<br>Cys<br>115 | Ala               | aca<br>Thr        | ggg<br>Gly        | ctc<br>Leu        | cag<br>Gln<br>120 | Val               | tct<br>Ser        | tat<br>Tyr        | ctg<br>Leu        | act<br>Thr<br>125 | Trp               | ggt<br>Gly        | gtg<br>Val        | 502  |
| ctg<br>Leu        | cag<br>Gln<br>130  | Glu               | aga<br>Arg        | gtg<br>Val        | atg<br>Met        | acc<br>Thr<br>135 | Arg               | agc<br>Ser        | tat<br>Tyr        | ggg<br>Gly        | gcc<br>Ala<br>140 | Thr               | gcc<br>Ala        | aca<br>Thr        | tca<br>Ser        | 550  |
| ccg<br>Pro<br>145 | Gly                | gag<br>Glu        | cgc<br>Arg        | ttt<br>Phe        | acg<br>Thr<br>150 | Asp               | tcg<br>Ser        | cag<br>G n        | ttc<br>Phe        | ctg<br>Leu<br>155 | Val               | cta<br>Leu        | atg<br>Met        | aac<br>Asn        | cga<br>Arg<br>160 | 598  |
| gtg<br>Val        | ctg<br>Leu         | gca<br>Ala        | ctg<br>Leu        | att<br>Ile<br>165 | gtg<br>Val        | gct<br>Ala        | ggc<br>Gly        | ctc<br>Leu        | tcc<br>Ser<br>170 | tgt<br>Cys        | gtt<br>Val        | ctc<br>Leu        | tgc<br>Cys        | aag<br>Lys<br>175 | cag<br>Gln        | 646  |
|                   |                    |                   |                   |                   |                   |                   |                   |                   |                   |                   | ttt<br>Phe        |                   |                   |                   |                   | 694  |
| aat<br>Asn        | gtg<br>Val         | ctt<br>Leu<br>195 | agc<br>Ser        | agc<br>Ser        | tgg<br>Trp        | tgc<br>Cys        | caa<br>Gln<br>200 | tac<br>Tyr        | gaa<br>Glu        | gct<br>Ala        | ctt<br>Leu        | aag<br>Lys<br>205 | ttc<br>Phe        | gtc<br>Val        | agc<br>Ser        | 742  |
| ttc<br>Phe        | ccc<br>Pro<br>210  | acc<br>Thr        | cag<br>G n        | gtg<br>Val        | ctg<br>Leu        | gcc<br>Ala<br>215 | aag<br>Lys        | gcc<br>Ala        | tct<br>Ser        | aag<br>Lys        | gtg<br>Val<br>220 | atc<br>Ile        | cct<br>Pro        | gtc<br>Val        | atg<br>Met        | 790  |
| ctg<br>Leu<br>225 | atg<br>Met         | gga<br>Gly        | aag<br>Lys        | ctt<br>Leu        | gtg<br>Val<br>230 | tct<br>Ser        | cgg<br>Arg        | cgc<br>Arg        | agc<br>Ser        | tac<br>Tyr<br>235 | gaa<br>Glu        | cac<br>His        | tgg<br>Trp        | gag<br>Glu        | tac<br>Tyr<br>240 | 838  |
| ctg<br>Leu        | aca<br>Thr         | gcc<br>Ala        | acc<br>Thr        | ctc<br>Leu<br>245 | Пe                | Ser               | Пe                | Gly               | Val               | Ser               | atg<br>Met        | Phe               | Leu               | cta<br>Leu<br>255 | tcc<br>Ser        | 886  |
| agc<br>Ser        | gga<br>Gly         | cca<br>Pro        | gag<br>Glu<br>260 | ccc<br>Pro        | cgc<br>Arg        | agc<br>Ser        | tcc<br>Ser        | cca<br>Pro<br>265 | gcc<br>Ala        | acc<br>Thr        | aca<br>Thr        | ctc<br>Leu        | tca<br>Ser<br>270 | ggc<br>Gly        | ctc<br>Leu        | 934  |
| atc<br>Ile        | tta<br>Leu         | ctg<br>Leu<br>275 | gca<br>Ala        | ggt<br>Gly        | tat<br>Tyr        | att<br>lle        | gct<br>Ala<br>280 | ttt<br>Phe        | gac<br>Asp        | agc<br>Ser        | ttc<br>Phe        | acc<br>Thr<br>285 | tca<br>Ser        | aac<br>Asn        | tgg<br>Trp        | 982  |
| cag<br>Gln        | gat<br>Asp<br>290  | gcc<br>Ala        | ctg<br>Leu        | ttt<br>Phe        | gcc<br>Ala        | tat<br>Tyr<br>295 | aag<br>Lys        | atg<br>Met        | tca<br>Ser        | tcg<br>Ser        | gtg<br>Val<br>300 | cag<br>Gln        | atg<br>Met        | atg<br>Met        | ttt<br>Phe        | 1030 |
| ggg<br>Gly<br>305 | gtc<br>Val         | aat<br>Asn        | ttc<br>Phe        | ttc<br>Phe        | tcc<br>Ser<br>310 | tgc<br>Cys        | ctc<br>Leu        | ttc<br>Phe        | Thr               | gtg<br>Val<br>315 | ggc<br>Gly        | tca<br>Ser        | ctg<br>Leu        | cta<br>Leu        | gaa<br>Glu<br>320 | 1078 |
| cag<br>Gin        | ggg<br>Gly         | gcc<br>Ala        | cta<br>Leu        | ctg<br>Leu        | gag<br>Glu        | gga<br>Gly        | acc<br>Thr        | cgc<br>Arg        | ttc<br>Phe        | atg<br>Met        | ggg<br>Gly        | cga<br>Arg        | cac<br>His        | agt<br>Ser        | gag<br>Glu        | 1126 |

|                          |                |                   |                   |                   |                   |            |                   |                   |                   |                   |            |                   | ,                 |                   |      |
|--------------------------|----------------|-------------------|-------------------|-------------------|-------------------|------------|-------------------|-------------------|-------------------|-------------------|------------|-------------------|-------------------|-------------------|------|
| ttt gc<br>Phe Al         | t gcc<br>a Ala | cat<br>His<br>340 | gcc<br>Ala        | ctg<br>Leu        | cta<br>Leu        | ctc<br>Leu | tcc<br>Ser<br>345 | atc<br>Ile        | tgc<br>Cys        | tcc<br>Ser        | gca<br>Ala | tgt<br>Cys<br>350 | ggc<br>Gly        | cag<br>Gln        | 1174 |
| ctc tte<br>Leu Phe       |                | Phe               |                   |                   |                   |            |                   |                   |                   |                   |            |                   |                   |                   | 1222 |
| atc atc<br>lle lle<br>37 | e Met          | acc<br>Thr        | ctc<br>Leu        | cgc<br>Arg        | cag<br>Gln<br>375 | gcc<br>Ala | ttt<br>Phe        | gcc<br>Ala        | atc<br>lle        | ctt<br>Leu<br>380 | ctt<br>Leu | tcc<br>Ser        | tgc<br>Cys        | ctt<br>Leu        | 1270 |
| ctc ta<br>Leu Ty<br>385  | t ggc<br>r Gly | cac<br>His        | act<br>Thr        | gtc<br>Val<br>390 | act<br>Thr        | gtg<br>Val | gtg<br>Val        | gga<br>Gly        | ggg<br>Gly<br>395 | ctg<br>Leu        | ggg<br>Gly | gtg<br>Val        | gct<br>Ala        | gtg<br>Val<br>400 | 1318 |
| gtc tt<br>Val Ph         | t gct<br>e Ala | gcc<br>Ala        | ctc<br>Leu<br>405 | ctg<br>Leu        | ctc<br>Leu        | aga<br>Arg | gtc<br>Val        | tac<br>Tyr<br>410 | gcg<br>Ala        | cgg<br>Arg        | ggc<br>Gly | cgt<br>Arg        | cta<br>Leu<br>415 | aag<br>Lys        | 1366 |
| caa cg<br>Gln Ar         | g gga<br>g Gly | aag<br>Lys<br>420 | aag<br>Lys        | gct<br>Ala        | gtg<br>Val        | cct<br>Pro | gtt<br>Val<br>425 | gag<br>Glu        | tct<br>Ser        | cct<br>Pro        | gtg<br>Val | cag<br>Gln<br>430 | aag<br>Lys        | gtt<br>Val        | 1414 |
| tgaggg                   | tgga           | aagg              | gcct              | ga gg             | gggt              | gaagt      | t gaa             | atag              | ggac              | ccto              | cca        | cca -             | tccc              | cttctg            | 1474 |
| ctgtaa                   | cctc           | tgag              | ggago             | ct gg             | gctga             | aaagg      | g gca             | aaaat             | tgca              | ggt               | gttt       | tct (             | cagta             | atcaca            | 1534 |
| gaccag                   | ctct           | gcago             | cagg              | gg at             | ttggg             | ggago      | c cca             | aggag             | ggca              | gcct              | ttcc       | ctt ·             | ttgc              | cttaag            | 1594 |
| tcaccc                   | atct           | tccaį             | gtaag             | gc ag             | gttta             | attct      | gag               | gccc              | ggg               | ggta              | agaca      | agt (             | octoa             | agtgag            | 1654 |
| gggttt                   | tggg           | gagt              | ttggg             | gg to             | caaga             | agago      | ata               | aggta             | aggt              | tcca              | acagt      | ta d              | ctctt             | сссас             | 1714 |
| aagtto                   | cctt           | aagto             | cttgo             | cc ct             | tagct             | gtgc       | tct               | gcca              | acct              | tcca              | agact      | ca o              | ctccc             | ctctg             | 1774 |
| caaata                   | cctg           | catt              | tctta             | ac co             | ctggt             | gaga       | a aaa             | agcad             | caag              | cggt              | tgtag      | ggc 1             | tccaa             | atgctg            | 1834 |
| ctttcc                   | cagg           | aggg              | tgaag             | ga tg             | ggtgo             | ctgtg      | g ctg             | gagga             | aaag              | ggga              | atgca      | aga (             | gccct             | gccca             | 1894 |
| gcacca                   | ccac           | ctcc              | tatgo             | ct co             | ctgga             | atcco      | c tag             | ggcto             | ctgt              | tcca              | atga       | gcc -             | tgttg             | gcaggt            | 1954 |
| tttggt                   | actt           | tagaa             | aatg              | ta ad             | cttt              | ttgct      | t ctt             | tataa             | attt              | tati              | ttta       | tta a             | aatta             | aaatta            | 2014 |
| ctgc                     |                |                   |                   |                   |                   |            |                   |                   |                   |                   |            |                   |                   |                   | 2018 |

<210> 87 <211> 235 <212> PRT

<213> Homo sapiens

Met Gly lle Gly Lys Ser Lys lle Asn Ser Cys Pro Leu Ser Leu Ser 1 5 10 15

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er Val Asp Thr Ser Pro Gly Tyr
Trp Gly Lys Arg Hi
Asp Ser Lys Lys Ser Glu Asp Leu Ser Leu Cys Asn Val Ala Glu His
Ser Asn Thr Thr Glu Gly Pro Thr Gly Lys Gln Glu Gly Ala Gln Ser
Val Glu Glu Met Phe Glu Glu Glu Ala Glu Glu Glu Val Phe Leu Lys
Phe Val IIe Leu His Ala Glu Asp Asp Thr Asp Glu Ala Leu Arg Val
Gin Asn Leu Leu Gin Asp Asp Phe Gly IIe Lys Pro Gly IIe IIe Phe
                                105
Ala Glu Met Pro Cys Gly Arg Gln His Leu Gln Asn Leu Asp Asp Ala
                            120
Val Asn Gly Ser Ala Trp Thr Ile Leu Leu Leu Thr Glu Asn Phe Leu
                        135
Arg Asp Thr Trp Cys Asn Phe Gln Phe Tyr Thr Ser Leu Met Asn Ser
                                         155
                    150
Val Asn Arg Gln His Lys Tyr Asn Ser Val Ile Pro Met Arg Pro Leu
                                    170
Asn Asn Pro Leu Pro Arg Glu Arg Thr Pro Phe Ala Leu Gln Thr Ile
                                185
Asn Ala Leu Glu Glu Glu Ser Arg Gly Phe Pro Thr Gln Val Glu Arg
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                                                 205
lle Phe Gln Glu Ser Val Tyr Lys Thr Gln Gln Thr lle Trp Lys Glu
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Thr Arg Asn Met Val Gln Arg Gln Phe lle Ala
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                                                                   116
aaatgctgag aaatacataa agttttcctc ttctgccttg gatatttata atg ggt
```

Met Gly

| atc<br>lle        | ggg<br>Gly        | aag<br>Lys<br>5   | tct<br>Ser        | aaa<br>Lys        | ata<br>He         | aat<br>Asn        | tcc<br>Ser<br>10  | tgc<br>Cys        | cct<br>Pro        | ctt<br>Leu        | tct<br>Ser        | ctc<br>Leu<br>15  | tct<br>Ser        | tgg<br>Trp        | ggt<br>Gly        | 164 |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-----|
| aaa<br>Lys        | agg<br>Arg<br>20  | cac<br>His        | agt<br>Ser        | gtg<br>Val        | gat<br>Asp        | aca<br>Thr<br>25  | agt<br>Ser        | cca<br>Pro        | gga<br>Gly        | tat<br>Tyr        | cat<br>His<br>30  | gag<br>Glu        | tca<br>Ser        | gat<br>Asp        | tcc<br>Ser        | 212 |
| aag<br>Lys<br>35  | aag<br>Lys        | tct<br>Ser        | gaa<br>Glu        | gat<br>Asp        | cta<br>Leu<br>40  | tcc<br>Ser        | ttg<br>Leu        | tgt<br>Cys        | aat<br>Asn        | gtt<br>Val<br>45  | gct<br>Ala        | gag<br>Glu        | cac<br>His        | agc<br>Ser        | aat<br>Asn<br>50  | 260 |
| aca<br>Thr        | aca<br>Thr        | gag<br>Glu        | ggg<br>Gly        | cca<br>Pro<br>55  | aca<br>Thr        | gga<br>Gly        | aag<br>Lys        | cag<br>Gln        | gag<br>Glu<br>60  | gga<br>Gly        | gct<br>Ala        | cag<br>Gln        | agc<br>Ser        | gtg<br>Val<br>65  | gaa<br>Glu        | 308 |
| gag<br>Glu        | atg<br>Met        | ttt<br>Phe        | gaa<br>Glu<br>70  | gaa<br>Glu        | gaa<br>Glu        | gct<br>Ala        | gaa<br>Glu        | gaa<br>Glu<br>75  | gag<br>Glu        | gtg<br>Val        | ttc<br>Phe        | ctc<br>Leu        | aaa<br>Lys<br>80  | ttt<br>Phe        | gtg<br>Val        | 356 |
| ata<br>He         | ttg<br>Leu        | cat<br>His<br>85  | gca<br>Ala        | gaa<br>Glu        | gat<br>Asp        | gac<br>Asp        | aca<br>Thr<br>90  | gat<br>Asp        | gaa<br>Glu        | gcc<br>Ala        | ctc<br>Leu        | aga<br>Arg<br>95  | gtc<br>Val        | cag<br>Gln        | aat<br>Asn        | 404 |
| ctg<br>Leu        | cta<br>Leu<br>100 | caa<br>Gln        | gat<br>Asp        | gac<br>Asp        | ttt<br>Phe        | ggt<br>Gly<br>105 | atc<br>Ile        | aaa<br>Lys        | ccc<br>Pro        | gga<br>Gly        | ata<br>Ile<br>110 | atc<br>Ile        | ttt<br>Phe        | gct<br>Ala        | gag<br>Glu        | 452 |
| atg<br>Met<br>115 | cca<br>Pro        | tgt<br>Cys        | ggc<br>Gly        | aga<br>Arg        | cag<br>Gln<br>120 | cat<br>His        | tta<br>Leu        | cag<br>Gln        | aat<br>Asn        | tta<br>Leu<br>125 | gat<br>Asp        | gat<br>Asp        | gct<br>Ala        | gta<br>Val        | aat<br>Asn<br>130 | 500 |
| ggg<br>Gly        | tct<br>Ser        | gca<br>Ala        | tgg<br>Trp        | aca<br>Thr<br>135 | atc<br>lle        | tta<br>Leu        | tta<br>Leu        | ctg<br>Leu        | act<br>Thr<br>140 | gaa<br>G u        | aac<br>Asn        | ttt<br>Phe        | tta<br>Leu        | aga<br>Arg<br>145 | gat<br>Asp        | 548 |
| act<br>Thr        | tgg<br>Trp        | tgt<br>Cys        | aat<br>Asn<br>150 | ttc<br>Phe        | cag<br>Gln        | ttc<br>Phe        | tat<br>Tyr        | acg<br>Thr<br>155 | tcc<br>Ser        | cta<br>Leu        | atg<br>Met        | aac<br>Asn        | tcc<br>Ser<br>160 | gtt<br>Val        | aac<br>Asn        | 596 |
| agg<br>Arg        | cag<br>Gln        | cat<br>His<br>165 | aaa<br>Lys        | tac<br>Tyr        | aac<br>Asn        | tct<br>Ser        | gtt<br>Val<br>170 | ata<br>He         | ccc<br>Pro        | atg<br>Met        | cgg<br>Arg        | ccc<br>Pro<br>175 | ctg<br>Leu        | aac<br>Asn        | aat<br>Asn        | 644 |
| ccc<br>Pro        | ctt<br>Leu<br>180 | ccc<br>Pro        | cga<br>Arg        | gaa<br>Glu        | agg<br>Arg        | act<br>Thr<br>185 | ccc<br>Pro        | ttt<br>Phe        | gcc<br>Ala        | ctc<br>Leu        | caa<br>Gln<br>190 | acc<br>Thr        | atc<br>Ile        | aat<br>Asn        | gcc<br>Ala        | 692 |
| tta<br>Leu<br>195 | gag<br>Glu        | gaa<br>Glu        | gaa<br>Glu        | agt<br>Ser        | cgt<br>Arg<br>200 | gga<br>Gly        | ttt<br>Phe        | cct<br>Pro        | aca<br>Thr        | caa<br>Gln<br>205 | gta<br>Val        | gaa<br>Glu        | aga<br>Arg        | att<br>Ile        | ttt<br>Phe<br>210 | 740 |
| cag<br>Gin        | gag<br>Glu        | tct<br>Ser        | gtg<br>Val        | tat<br>Tyr<br>215 | aag<br>Lys        | aca<br>Thr        | caa<br>Gln        | caa<br>Gln        | act<br>Thr<br>220 | Пe                | tgg<br>Trp        | aaa<br>Lys        | gag<br>Glu        | aca<br>Thr<br>225 | aga<br>Arg        | 788 |
| aat               | atg               | gta               | caa               | aga               | caa               | ttt               | att               | gcc               | tga               | gatg              | aaa               | cata              | taac              | at                |                   | 835 |

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Val lle Leu Leu Ala Val Gly lle Trp Gly Lys Val Ser Leu Glu Asn 35 40 45

Tyr Phe Ser Leu Leu Asn Glu Lys Ala Thr Asn Val Pro Phe Val Leu 50 60

lle Ala Thr Gly Thr Val lle lle Leu Leu Gly Thr Phe Gly Cys Phe 65 70 75 80

Ala Thr Cys Arg Ala Ser Ala Trp Met Leu Lys Leu Tyr Ala Met Phe 85 90 95

Leu Thr Leu Val Phe Leu Val Glu Leu Val Ala Ala Ile Val Gly Phe 100 105 110

Val Phe Arg His Glu lle Lys Asn Ser Phe Lys Asn Asn Tyr Glu Lys 115 120 125

Ala Leu Lys Gln Tyr Asn Ser Thr Gly Asp Tyr Arg Ser His Ala Val

Asp Lys lle Gln Asn Thr Leu His Cys Cys Gly Val Thr Asp Tyr Arg 145 150 155 160

Asp Trp Thr Asp Thr Asn Tyr Tyr Ser Glu Lys Gly Phe Pro Lys Ser 165 170 175

Cys Cys Lys Leu Giu Asp Cys Thr Pro Gin Arg Asp Ala Asp Lys Val 180 185 190

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| gat tgg aca gat act aat tat tac tca gaa aaa gga ttt cct aag agt 58<br>Asp Trp Thr Asp Thr Asn Tyr Tyr Ser Glu Lys Gly Phe Pro Lys Ser<br>165 170 175     | 37         |
|--|------------|
| tgc tgt aaa ctt gaa gat tgt act cca cag aga gat gca gac aaa gta 63<br>Cys Cys Lys Leu Glu Asp Cys Thr Pro Gln Arg Asp Ala Asp Lys Val<br>180 185 190     | ł5         |
| aac aat gaa ggt tgt ttt ata aag gtg atg acc att ata gag tca gaa 68<br>Asn Asn Glu Gly Cys Phe lle Lys Vai Met Thr lle lle Glu Ser Glu<br>195 200 205     | 13         |
| atg gga gtc gtt gca gga att tcc ttt gga gtt gct tgc ttc caa ctg 73<br>Met Gly Val Val Ala Gly Ile Ser Phe Gly Val Ala Cys Phe Gln Leu<br>210 215 220     | .1         |
| att gga atc ttt ctc gcc tac tgc ctc tct cgt gcc ata aca aat aac 77<br>lle Gly lle Phe Leu Ala Tyr Cys Leu Ser Arg Ala lle Thr Asn Asn<br>225 230 235 240 | 9          |
| cag tat gag ata gtg taacccaatg tatctgtggg cctattcctc tctaccttta 83<br>Gln Tyr Glu lle Val<br>245   | 4          |
| aggacattta gggtcccccc tgtgaattag aaagttgctt ggctggagaa ctgacaacac 89   | 4          |
| tacttactga tagaccaaaa aactacacca gtaggttgat tcaatcaaga tgtatgtaga 954  | 4          |
| cctaaaacta caccaatagg ctgattcaat caagatccgt gctcgcagtg ggctgattca 10   | 14         |
| atcaagatgt atgtttgcta tgttctaagt ccaccttcta tcccattcat gttagatcgt 10   | 74         |
| tgaaaccctg tatccctctg aaacactgga agagctagta aattgtaaat gaagtaatac 113  | 34         |
| tgtgttcctc ttgactgtta tttttcttag tagggggcct ttggaaggca ctgtgaattt 119  | 94         |
| gctattttga tgtagtgtta caagatggaa aattgattcc tctgactttg ctattgatgt 125  | 54         |
| agtgtgatag aaaattcacc cctctgaact ggctccttcc cagtcaaggt tatctggttt 131  | 14         |
| gattgtataa tttgcaccaa gaagttaaaa tgttttatga ctctctgttc tgctgacagg 137  | 74         |
| cagagagtca cattgtgtaa tttaatttca gtcagtcaat agatggcatc cctcatcagg 143  | 34         |
| gttgccagat ggtgataaca gtgtaaggcc ttgggtctaa ggcatccacg actggaaggg 149  | <b>)</b> 4 |
| actactgatg ttctgtgata catcaggttt cagcacacaa cttacatttc tttgcctcca 155  | 54         |
| aattgaggca tttattatga tgttcatact ttccctcttg tttgaaagtt tctaattatt 161  | 4          |
| aaatggtgtc ggaattgttg tattttcctt aggaattcag tggaacttat cttcattaaa 167  | 14         |
| tttagctggt accaggttga tatgacttgt caatattatg gtcaacttta agtcttagtt 173  | . 4        |
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Asn Ser Glu Ala Cys Arg Asp Gly Leu Arg Ala Val Met Glu Cys Arg
Asn Val Thr His Leu Leu Gln Gln Glu Leu Thr Glu Ala Gln Lys Gly
Phe Gin Asp Val Glu Ala Gln Ala Ala Thr Cys Asn His Thr Val Met
Ala Leu Met Ala Ser Leu Asp Ala Glu Lys Ala Gln Gly Gln Lys Lys
                                 105
Val Glu Glu Leu Glu Gly Glu Ile Thr Thr Leu Asn His Lys Leu Gln
                             120
Asp Ala Ser Ala Glu Val Glu Arg Leu Arg Arg Glu Asn Gln Val Leu
                        135
Ser Val Arg lie Ala Asp Lys Lys Tyr Tyr Pro Ser Ser Gin Asp Ser
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Ser Ser Ala Ala Ala Pro Gln Leu Leu Ile Val Leu Leu Gly Leu Ser
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100

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| Arg Val Pro Met Glop Gly Asp Lys Arg Cys Lys Leu Leu Gly 10 25  |     |
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| ata gga att ctg gtg ctc ctg atc atc gtg att ctg ggg gtg ccc ttg<br>  e G y   e Leu Val Leu Leu   e   e Val   e Leu G y Val Pro Leu<br>30 35 40      | 148 |
| att atc ttc acc atc aag gcc aac agc gag gcc tgc cgg gac ggc ctt<br>lle lle Phe Thr lle Lys Ala Asn Ser Glu Ala Cys Arg Asp Gly Leu<br>45 50 55      | 196 |
| cgg gca gtg atg gag tgt cgc aat gtc acc cat ctc ctg caa caa gag<br>Arg Ala Val Met Glu Cys Arg Asn Val Thr His Leu Leu Gln Gln<br>60 65 70          | 244 |
| ctg acc gag gcc cag aag ggc ttt cag gat gtg gag gcc cag gct gcc<br>Leu Thr Glu Ala Gln Lys Gly Phe Gln Asp Val Glu Ala Gln Ala Ala<br>75 80 85      | 292 |
| acc tgc aac cac act gtg atg gcc cta atg gct tcc ctg gat gca gag<br>Thr Cys Asn His Thr Val Met Ala Leu Met Ala Ser Leu Asp Ala Glu<br>90 95 100 105 | 340 |
| aag gcc caa gga caa aag aaa gtg gag gag ctt gag gga gag atc act<br>Lys Ala Gin Giy Gin Lys Lys Val Giu Giu Leu Giu Giy Giu ile Thr<br>110 115 120   | 388 |
| aca tta aac cat aag ctt cag gac gcg tct gca gag gtg gag cga ctg<br>Thr Leu Asn His Lys Leu Gln Asp Ala Ser Ala Glu Val Glu Arg Leu<br>125 130 135   | 436 |
| aga aga gaa aac cag gtc tta agc gtg aga atc gcg gac aag aag tac<br>Arg Arg Glu Asn Gln Val Leu Ser Val Arg Ile Ala Asp Lys Lys Tyr<br>140 145 150   | 484 |
| tac ccc agc tcc cag gac tcc agc tcc gct gcg gcg ccc cag ctg ctg<br>Tyr Pro Ser Ser Gln Asp Ser Ser Ser Ala Ala Ala Pro Gln Leu Leu<br>155 160 165   | 532 |
| att gtg ctg ctg ggc ctc agc gct ctg ctg cag tgagatccca ggaagctggc<br>lie Val Leu Leu Gly Leu Ser Ala Leu Leu Gln<br>170 175 180                     | 585 |
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| ttctgagcgg gtcatggggc aacacggtta gcggggagag cacggggtag ccggagaagg   | 705 |
| gcctctggag caggtctgga ggggccatgg ggcagtcctg ggtgtgggga cacagtcggg   | 765 |
| ttgacccagg gctgtctccc tccagagcct ccctccggac aatgagtccc ccctcttgtc   | 825 |
| tcccaccctg agattgggca tggggtgcgg tgtggggggc atgtgctgcc tgttgttatg   | 885 |
| ggttttttt gcggggggg ttgcttttt ctggggtctt tgagctccaa aaaataaaca  | 945 |
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Ala Asp Ala Leu Tyr Glu Ala Leu Lys Lys Leu Arg Thr Tyr Ala Ala 50 55 60

lle Glu Asp Glu Tyr Val Gin Gin Lys Asp Glu Gin Phe Arg Glu Trp 65 70 75 80

Phe Leu Lys Glu Phe Pro Gln Val Lys Arg Lys Ile Gln Glu Ser Ile 85 90 95

Glu Lys Leu Arg Ala Leu Ala Asn Gly Ile Glu Glu Val His Arg Gly 100 105 110

Cys Thr lie Ser Asn Val Val Ser Ser Ser Thr Gly Ala Ala Ser Gly 115 120 125

lle Met Ser Leu Ala Gly Leu Val Leu Ala Pro Phe Thr Ala Gly Thr 130 135 140

Ser Leu Ala Leu Thr Ala Ala Gly Val Gly Leu Gly Ala Ala Ser Ala 145 150 155 160

Val Thr Gly 11e Thr Thr Ser 11e Val Glu His Ser Tyr Thr Ser Ser 165 170 175

Ala Glu Ala Glu Ala Ser Arg Leu Thr Ala Thr Ser Ile Asp Arg Leu 180 185 190

Lys Val Phe Lys Glu Val Met Arg Asp IIe Thr Pro Asn Leu Leu Ser 195 200 205

Leu Leu Asn Asn Tyr Tyr Glu Ala Thr Gln Thr Ile Gly Ser Glu Ile 210 215 220

Arg Ala lle Arg Gln Ala Arg Ala Arg Leu Pro Val Thr Thr 225 230 235 240

Trp Arg lie Ser Ala Gly Ser Gly Gly Gln Ala Glu Arg Thr Ile Ala 245 250 255

Gly Thr Thr Arg Ala Val Ser Arg Gly Ala Arg Ile Leu Ser Ala Thr 260 265 270

Thr Ser Gly Ile Phe Leu Ala Leu Asp Val Val Asn Leu Val Tyr Glu



285

Ser Lys His Leu His Glu Gly Ala Lys Ser Ala Ser Ala Glu Glu Leu 290 295 300

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tcagtgactg gagageteca aggaaagtet etcagtgace tggetgetgg cace atg 177
Met

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gag aga gtc agc cca gtg cat ctg caa atc ctg ctg act aac aat gaa 273 Glu Arg Val Ser Pro Val His Leu Gln Ile Leu Leu Thr Asn Asn Glu 20 25 30

gcc tgg aag aga ttc gtg act gcg gct gaa ttg ccc agg gat gag gca 321 Ala Trp Lys Arg Phe Val Thr Ala Ala Glu Leu Pro Arg Asp Glu Ala 35 40 45

gat gct ctc tac gaa gct ctg aag aag ctt aga aca tat gca gct att 369 Asp Ala Leu Tyr Glu Ala Leu Lys Lys Leu Arg Thr Tyr Ala Ala lie 50 55 60 65

gag gac gaa tat gtg cag cag aaa gat gag cag ttt agg gaa tgg ttt 417 Glu Asp Glu Tyr Val Gln Gln Lys Asp Glu Gln Phe Arg Glu Trp Phe 70 75 80

ttg aaa gag ttt ccc caa gtc aag agg aag atc cag gag tcc ata gaa 465 Leu Lys Glu Phe Pro Gln Val Lys Arg Lys I!e Gln Glu Ser IIe Glu 85 90 95

aag ctt cgt gcc ctt gca aat ggt att gaa gag gtc cac aga ggc tgc 513 Lys Leu Arg Ala Leu Ala Asn Gly Ile Glu Glu Val His Arg Gly Cys 100 105 110

| acc<br>Thr        | atc<br>  e<br> 115 | Ser               | aac<br>Asn        | gt<br>Val         | t g<br>Val        | tcc<br>Ser<br>120 | Ser               | tcc<br>Ser        | act<br>Thr        | ggc<br>Gly        | gct<br>Ala<br>125 | Ala               | Ser               | ggc<br>Gly        | atc<br>Ile        | 561  |
|-------------------|--------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| atg<br>Met<br>130 | Ser                | ctt<br>Leu        | gct<br>Ala        | ggt<br>Gly        | ctt<br>Leu<br>135 | gtt<br>Val        | ttg<br>Leu        | gca<br>Ala        | cca<br>Pro        | ttt<br>Phe<br>140 | Thr               | gca<br>Ala        | ggg<br>Gly        | acg<br>Thr        | agt<br>Ser<br>145 | 609  |
| ctg<br>Leu        | gcc<br>Ala         | ctt<br>Leu        | act<br>Thr        | gca<br>Ala<br>150 | gct<br>Ala        | ggg<br>Gly        | gta<br>Val        | ggg<br>Gly        | ctg<br>Leu<br>155 | Gly               | gca<br>Ala        | gcg<br>Ala        | tct<br>Ser        | gct<br>Ala<br>160 | gtg<br>Val        | 657  |
| act<br>Thr        | ggg<br>Gly         | atc<br>lle        | acc<br>Thr<br>165 | acc<br>Thr        | agc<br>Ser        | atc<br>Ile        | gtg<br>Val        | gag<br>Glu<br>170 | cac<br>His        | tca<br>Ser        | tac<br>Tyr        | aca<br>Thr        | tca<br>Ser<br>175 | tca<br>Ser        | gca<br>Ala        | 705  |
| gaa<br>Glu        | gct<br>Ala         | gaa<br>Glu<br>180 | Ala               | agc<br>Ser        | agg<br>Arg        | ctg<br>Leu        | act<br>Thr<br>185 | gca<br>Ala        | acc<br>Thr        | agc<br>Ser        | att<br>Ile        | gac<br>Asp<br>190 | cga<br>Arg        | ttg<br>Leu        | aag<br>Lys        | 753  |
| gta<br>Val        | ttt<br>Phe<br>195  | aag<br>Lys        | gaa<br>Glu        | gtt<br>Val        | atg<br>Met        | cgt<br>Arg<br>200 | gac<br>Asp        | atc<br>lle        | aca<br>Thr        | ccc<br>Pro        | aac<br>Asn<br>205 | tta<br>Leu        | ctt<br>Leu        | tcc<br>Ser        | ctt<br>Leu        | 801  |
| ctt<br>Leu<br>210 | Asn                | aat<br>Asn        | tat<br>Tyr        | tac<br>Tyr        | gaa<br>Glu<br>215 | gcc<br>Ala        | aca<br>Thr        | caa<br>Gln        | acc<br>Thr        | att<br>  e<br>220 | ggg<br>Gly        | agt<br>Ser        | gaa<br>Glu        | atc<br>Ile        | cgt<br>Arg<br>225 | 849  |
| gcc<br>Ala        | atc<br>lle         | agg<br>Arg        | caa<br>Gln        | gcc<br>Ala<br>230 | aga<br>Arg        | gcc<br>Ala        | agg<br>Arg        | gcc<br>Ala        | cga<br>Arg<br>235 | ctc<br>Leu        | cct<br>Pro        | gtg<br>Val        | acc<br>Thr        | acc<br>Thr<br>240 | tgg<br>Trp        | 897  |
| cga<br>Arg        | atc<br>lle         | tca<br>Ser        | gct<br>Ala<br>245 | gga<br>Gly        | agt<br>Ser        | ggt<br>Gly        | ggt<br>Gly        | caa<br>Gin<br>250 | gca<br>Ala        | gag<br>Glu        | aga<br>Arg        | acg<br>Thr        | att<br>11e<br>255 | gca<br>Ala        | ggc<br>Gly        | 945  |
| acc<br>Thr        | acc<br>Thr         | cgg<br>Arg<br>260 | gca<br>Ala        | gtg<br>Val        | agc<br>Ser        | aga<br>Arg        | gga<br>Gly<br>265 | gcc<br>Ala        | cgg<br>Arg        | atc<br>Ile        | ctg<br>Leu        | agt<br>Ser<br>270 | gcg<br>Ala        | acc<br>Thr        | act<br>Thr        | 993  |
| tca<br>Ser        | ggc<br>Gly<br>275  | atc<br>lle        | ttc<br>Phe        | ctt<br>Leu        | gca<br>Ala        | ctg<br>Leu<br>280 | gat<br>Asp        | gtg<br>Val        | gtc<br>Val        | aac<br>Asn        | ctt<br>Leu<br>285 | gta<br>Val        | tac<br>Tyr        | gag<br>Glu        | tca<br>Ser        | 1041 |
| aag<br>Lys<br>290 | cac<br>His         | ttg<br>Leu        | cat<br>His        | gag<br>Glu        | ggg<br>Gly<br>295 | gca<br>Ala        | aag<br>Lys        | tct<br>Ser        | gca<br>Ala        | tct<br>Ser<br>300 | gct<br>Ala        | gag<br>Glu        | gag<br>Glu        | ctg<br>Leu        | agg<br>Arg<br>305 | 1089 |
| cgg<br>Arg        | cag<br>Gln         | gct<br>Ala        | cag<br>Gln        | gag<br>Glu<br>310 | ctg<br>Leu        | gag<br>Glu        | gag<br>Glu        | Asn               | cta<br>Leu<br>315 | atg<br>Met        | gag<br>Glu        | ctc<br>Leu        | Thr               | cag<br>Gln<br>320 | atc<br>lle        | 1137 |
| tat<br>Tyr        | cag<br>Gln         | cgt<br>Arg        | ctg<br>Leu<br>325 | aat<br>Asn        | cca<br>Pro        | tgc<br>Cys        | His               | acc<br>Thr<br>330 | cac<br>His        | tgac              | ссса              | ga c              | cagt              | gcag              | С                 | 1187 |

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Pro Ala Pro Phe Lys Cys Pro Thr Cys Arg Lys Glu Thr Ser Ala Thr 50 55 60

Gly lle Asn Ser Leu Gln Val Asn Tyr Ser Leu Lys Gly lle Val Glu 65 70 75 80

Lys Tyr Asn Lys IIe Lys IIe Ser Pro Lys Met Pro Val Cys Lys Gly 85 90 95

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<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

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|            |                   |            |            |            |            | aag<br>Lys        |            |            |            |            |                   |            |            |            |            | 756  |
|------------|-------------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|------|
|            |                   |            |            |            |            | gaa<br>Glu        |            |            |            |            |                   |            |            |            |            | 804  |
|            |                   |            |            |            |            | tat<br>Tyr<br>215 |            |            |            |            |                   |            |            |            |            | 852  |
|            |                   |            |            |            |            | atg<br>Met        |            |            |            |            |                   |            |            |            |            | 900  |
|            |                   |            |            |            |            | gta<br>Val        |            |            |            |            |                   |            |            |            |            | 948  |
|            |                   |            |            |            |            | aag<br>Lys        |            |            |            |            |                   |            |            |            |            | 996  |
|            |                   |            |            |            |            | aag<br>Lys        |            |            |            |            |                   |            |            |            |            | 1044 |
|            |                   |            |            |            |            | gat<br>Asp<br>295 |            |            |            |            |                   |            |            |            |            | 1092 |
|            |                   |            |            |            |            | ccc<br>Pro        |            |            |            |            |                   |            |            |            |            | 1140 |
|            |                   |            | Leu        |            | Leu        | gtc<br>Val        |            | ΫaΙ        | Phe        | Gly        |                   |            |            |            | Leu        | 1188 |
|            |                   |            |            |            |            | gac<br>Asp        |            |            |            |            |                   |            |            |            |            | 1236 |
|            |                   |            |            |            |            | act<br>Thr        |            |            |            |            |                   |            |            |            |            | 1284 |
| gtt<br>Val | ttt<br>Phe<br>370 | tac<br>Tyr | tgg<br>Trp | gaa<br>Glu | cag<br>G n | gtg<br>Val<br>375 | aca<br>Thr | gat<br>Asp | ggg<br>Gly | ttt<br>Phe | ttc<br>Phe<br>380 | att<br>Ile | ttc<br>Phe | aat<br>Asn | gaa<br>Glu | 1332 |
|            |                   |            |            |            |            | ttg<br>Leu        |            |            |            |            |                   |            |            |            |            | 1380 |
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Gln Lys Gln Leu Arg Gln Glu Thr Phe Cys Cys Pro Gln Cys Arg Ala 50 55 60

Pro Phe His Met Asp Ser Leu Arg Pro Asn Lys Gln Leu Gly Ser Leu 65 70 75 80

lle Glu Ala Leu Lys Glu Thr Asp Gln Glu Met Ser Cys Glu Glu His 85 90 95

Gly Glu Gln Phe His Leu Phe Cys Glu Asp Glu Gly Gln Leu lle Cys 100 105 110

Trp Arg Cys Glu Arg Ala Pro Gln His Lys Gly His Thr Thr Ala Leu 115 120 125

Val Glu Asp Val Cys Gln Gly Tyr Lys Glu Lys Leu Gln Glu Ala Val 130 135 140

Thr Lys Leu Lys Gln Leu Glu Asp Arg Cys Thr Glu Gln Lys Leu Ser 145 150 155 160

Thr Ala Met Arg Ile Thr Lys Trp Lys Glu Lys Val Gln Ile Gln Arg 165 170 175

Gln Lys Ile Arg Ser Asp Phe Lys Asn Leu Gln Cys Phe Leu His Glu 180 185 190

Glu Glu Lys Ser Tyr Leu Trp Arg Leu Glu Lys Glu Glu Gln Gln Thr 195 200 205

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Glu Leu Lys Ser His lle Leu Glu Leu Glu Glu Lys Cys Gln Gly Ser 225 230 235 240

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Ala Val Lys Leu Glu Thr Ser Glu Ala Val Ser Leu Glu Leu His Thr



Met Cys Asn Val Ser Lys Leu Tyr Phe Asp Val Lys Lys Met Leu Arg 275 280 285

Ser His Gln Val Ser Val Thr Leu Asp Pro Asp Thr Ala His His Glu 290 295 300

Leu lle Leu Ser Glu Asp Arg Arg Gln Val Thr Arg Gly Tyr Thr Gln 305 310 315 320

Glu Asn Gln Asp Thr Ser Ser Arg Arg Phe Thr Ala Phe Pro Cys Val 325 330 335

Leu Gly Cys Glu Gly Phe Thr Ser Gly Arg Arg Tyr Phe Glu Val Asp 340 345 350

Val Gly Glu Gly Thr Gly Trp Asp Leu Gly Val Cys Met Glu Asn Val 355 360 365

Gln Arg Gly Thr Gly Met Lys Gln Glu Pro Gln Ser Gly Phe Trp Thr 370 375 380

Leu Arg Leu Cys Lys Lys Gly Tyr Val Ala Leu Thr Ser Pro Pro 385 390 395 400

Thr Ser Leu His Leu His Glu Gln Pro Leu Leu Val Gly IIe Phe Leu 405 410 415

Asp Tyr Glu Ala Gly Val Val Ser Phe Tyr Asn Gly Asn Thr Gly Cys 420 425 430

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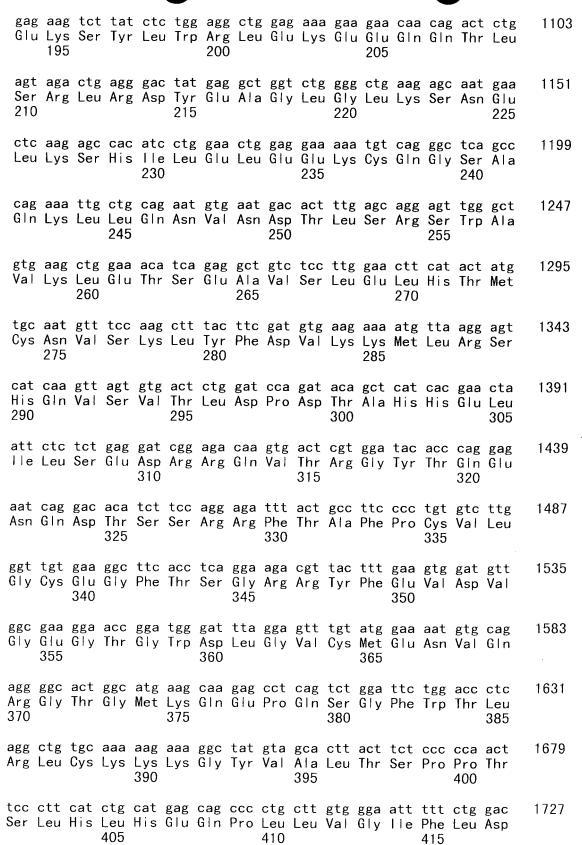
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| tcaatacaaa a                      | tgagataat ag                      | ggggttgga ag                      | gaaaacct                      | tcaagaccta                        | tggaagtcag                | 360  |
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| atc tgc ctg<br>lle Cys Leu<br>20  | agc ctg atg<br>Ser Leu Met        | acg aac cca<br>Thr Asn Pro<br>25  | a gta agc<br>Val Ser          | atc aac tgt<br>lle Asn Cys<br>30  | gga cac<br>Gly His        | 575  |
| agc tac tgc<br>Ser Tyr Cys<br>35  | cac ttg tgt<br>His Leu Cys        | ata aca gad<br>lle Thr Asp<br>40  | ttc ttt<br>Phe Phe            | aaa aac cca<br>Lys Asn Pro<br>45  | agc caa<br>Ser Gln        | 623  |
| aag caa ctg<br>Lys Gln Leu<br>50  | agg cag gag<br>Arg Gln Glu<br>55  | aca ttc tgo<br>Thr Phe Cys        | tgt ccc<br>Cys Pro<br>60      | cag tgt cgg<br>Gln Cys Arg        | gct cca<br>Ala Pro<br>65  | 671  |
| ttt cat atg<br>Phe His Met        | gat agc ctc<br>Asp Ser Leu<br>70  | cga ccc aad<br>Arg Pro Asr        | aag cag<br>Lys Gin<br>75      | ctg gga agc<br>Leu Gly Ser        | ctc att<br>Leu IIe<br>80  | 719  |
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| gag cag ttc<br>Glu Gln Phe<br>100 | His Leu Phe                       | tgc gaa gad<br>Cys Glu Asp<br>105 | Glu Gly                       | Gln Leu lle                       | tgc tgg<br>Cys Trp        | 815  |
| cgc tgt gag<br>Arg Cys Glu<br>115 | cgg gca cca<br>Arg Ala Pro        | cag cac aaa<br>Gln His Lys<br>120 | a ggg cac<br>s Gly His        | acc aca gct<br>Thr Thr Ala<br>125 | ctt gtt<br>Leu Val        | 863  |
| gaa gac gta<br>Glu Asp Val<br>130 | tgc cag ggc<br>Cys Gln Gly<br>135 | tac aag gaa<br>Tyr Lys Glu        | a aag ctc<br>u Lys Leu<br>140 | cag gaa gct<br>Gin Giu Ala        | gtg aca<br>Val Thr<br>145 | 911  |
| aaa ctg aag<br>Lys Leu Lys        | caa ctt gaa<br>Gln Leu Glu<br>150 | gac aga tg<br>Asp Arg Cys         | t acg gag<br>s Thr Glu<br>155 | cag aag ctg<br>GIn Lys Leu        | tcc aca<br>Ser Thr<br>160 | 959  |
| gca atg cga<br>Ala Met Arg        | ata act aaa<br>lle Thr Lys<br>165 | tgg aaa gag<br>Trp Lys Glu<br>170 | ı Lys Val                     | cag att cag<br>Gin Ile Gin<br>175 | aga caa<br>Arg Gln        | 1007 |
| aaa atc cgg<br>Lys Ile Arg        | tct gac ttt<br>Ser Asp Phe        | aag aat cto<br>Lys Asn Lei        | c cag tgt<br>u Gln Cys        | ttc cta cat<br>Phe Leu His        | gag gaa<br>Glu Glu        | 1055 |



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Glu Glu Lys Ser Tyr Leu Trp Arg Leu Glu Lys Glu Glu Gln Gln Thr 200 Leu Ser Arg Leu Arg Asp Tyr Glu Ala Gly Leu Gly Leu Lys Ser Asn Glu Leu Lys Ser His Ile Leu Glu Leu Glu Glu Lys Cys Gln Gly Ser 225 230 Ala Gln Lys Leu Leu Gln Asn Val Asn Asp Thr Leu Ser Arg Ser Trp Ala Val Lys Leu Glu Thr Ser Glu Ala Val Ser Leu Glu Leu His Thr Met Cys Asn Val Ser Lys Leu Tyr Phe Asp Val Lys Lys Met Leu Arg Ser His Gln Val Ser Val Thr Leu Asp Pro Asp Thr Ala His His Glu 295 Leu lle Leu Ser Glu Asp Arg Arg Gln Val Thr Arg Gly Tyr Thr Gln 305 315 Glu Asn Gin Asp Thr Ser Ser Arg Arg Phe Thr Ala Phe Pro Cys Val 325 Leu Gly Cys Glu Gly Phe Thr Ser Gly Arg Arg Tyr Phe Glu Val Asp 345 Val Gly Glu Gly Thr Gly Trp Asp Leu Gly Val Cys Met Glu Asn Val 365 Gln Arg Gly Thr Gly Met Lys Gln Glu Pro Gln Ser Gly Phe Trp Thr 375 Leu Arg Leu Cys Lys Lys Gly Tyr Val Ala Leu Thr Ser Pro Pro Thr Ser Leu His Leu His Glu Gln Pro Leu Leu Val Gly lle Phe Leu 405 Asp Tyr Glu Ala Gly Val Val Ser Phe Tyr Asn Gly Asn Thr Gly Cys 425 His Ile Phe Thr Phe Pro Lys Ala Ser Phe Ser Asp Thr Leu Arg Pro 435 445 Tyr Phe Gin Val Tyr Gln Tyr Ser Pro Leu Phe Leu Pro Pro Pro Gly 450 455

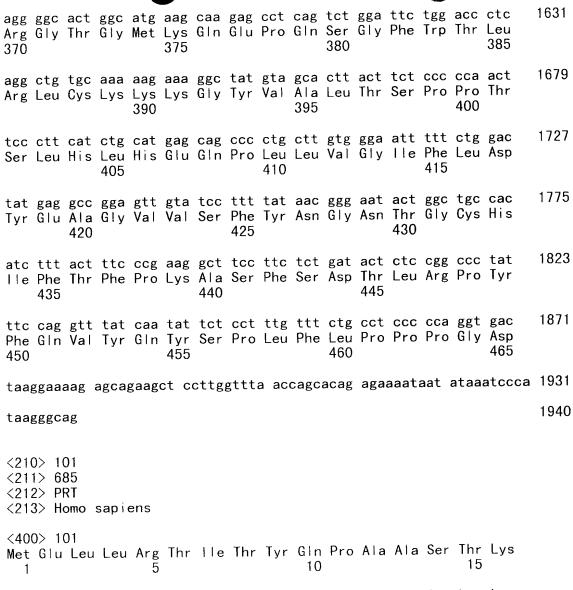
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| gaa<br>Glu<br>130 | gac<br>Asp        | gta<br>Val        | tgc<br>Cys        | ca.<br>Gln        | c<br>Gly<br>135   | tac<br>Tyr         | aag<br>Lys        | gaa<br>Glu        | aag<br>Lys        | ctc<br>Leu<br>140 | cag<br>G n        | aaa<br>Lys        | _                 | gtg<br>Val        |                   | 911  |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|--------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| aaa<br>Lys        | ctg<br>Leu        | aag<br>Lys        | caa<br>Gln        | ctt<br>Leu<br>150 | gaa<br>Glu        | gac<br>Asp         | aga<br>Arg        | tgt<br>Cys        | acg<br>Thr<br>155 | gag<br>Glu        | cag<br>Gln        | aag<br>Lys        | ctg<br>Leu        | tcc<br>Ser<br>160 | aca<br>Thr        | 959  |
| gca<br>Ala        | atg<br>Met        | cga<br>Arg        | ata<br>  e<br>165 | act<br>Thr        | aaa<br>Lys        | tgg<br>Trp         | aaa<br>Lys        | gag<br>Glu<br>170 | aag<br>Lys        | gta<br>Val        | cag<br>G n        | att<br>Ile        | cag<br>Gln<br>175 | aga<br>Arg        | caa<br>Gln        | 1007 |
| aaa<br>Lys        | atc<br>Ile        | cgg<br>Arg<br>180 | tct<br>Ser        | gac<br>Asp        | ttt<br>Phe        | aag<br>Lys         | aat<br>Asn<br>185 | ctc<br>Leu        | cag<br>Gln        | tgt<br>Cys        | ttc<br>Phe        | cta<br>Leu<br>190 | cat<br>His        | gag<br>Glu        | gaa<br>Glu        | 1055 |
| gag<br>Glu        | aag<br>Lys<br>195 | tct<br>Ser        | tat<br>Tyr        | ctc<br>Leu        | tgg<br>Trp        | agg<br>Arg<br>200  | ctg<br>Leu        | gag<br>Glu        | aaa<br>Lys        | gaa<br>Glu        | gaa<br>Glu<br>205 | caa<br>Gln        | cag<br>Gln        | act<br>Thr        | ctg<br>Leu        | 1103 |
| agt<br>Ser<br>210 | aga<br>Arg        | ctg<br>Leu        | agg<br>Arg        | gac<br>Asp        | tat<br>Tyr<br>215 | g <b>ag</b><br>Glu | gct<br>Ala        | ggt<br>Gly        | ctg<br>Leu        | ggg<br>Gly<br>220 | ctg<br>Leu        | aag<br>Lys        | agc<br>Ser        | aat<br>Asn        | gaa<br>Glu<br>225 | 1151 |
| ctc<br>Leu        | aag<br>Lys        | agc<br>Ser        | cac<br>His        | atc<br>lle<br>230 | ctg<br>Leu        | gaa<br>Glu         | ctg<br>Leu        | gag<br>Glu        | gaa<br>Glu<br>235 | aaa<br>Lys        | tgt<br>Cys        | cag<br>Gln        | ggc<br>Gly        | tca<br>Ser<br>240 | gcc<br>Ala        | 1199 |
| cag<br>Gln        | aaa<br>Lys        | ttg<br>Leu        | ctg<br>Leu<br>245 | cag<br>Gln        | aat<br>Asn        | gtg<br>Val         | aat<br>Asn        | gac<br>Asp<br>250 | act<br>Thr        | ttg<br>Leu        | agc<br>Ser        | agg<br>Arg        | agt<br>Ser<br>255 | tgg<br>Trp        | gct<br>Ala        | 1247 |
| gtg<br>Val        | aag<br>Lys        | ctg<br>Leu<br>260 | gaa<br>Glu        | aca<br>Thr        | tca<br>Ser        | gag<br>Glu         | gct<br>Ala<br>265 | gtc<br>Val        | tcc<br>Ser        | ttg<br>Leu        | gaa<br>Glu        | ctt<br>Leu<br>270 | cat<br>His        | act<br>Thr        | atg<br>Met        | 1295 |
| tgc<br>Cys        | aat<br>Asn<br>275 | gtt<br>Val        | tcc<br>Ser        | aag<br>Lys        | ctt<br>Leu        | tac<br>Tyr<br>280  | ttc<br>Phe        | gat<br>Asp        | gtg<br>Val        | aag<br>Lys        | aaa<br>Lys<br>285 | atg<br>Met        | tta<br>Leu        | agg<br>Arg        | agt<br>Ser        | 1343 |
| cat<br>His<br>290 | caa<br>G n        | gtt<br>Val        | agt<br>Ser        | gtg<br>Val        | act<br>Thr<br>295 | ctg<br>Leu         | gat<br>Asp        | cca<br>Pro        | gat<br>Asp        | aca<br>Thr<br>300 | gct<br>Ala        | cat<br>His        | cac<br>His        | gaa<br>Glu        | cta<br>Leu<br>305 | 1391 |
| att<br>He         | ctc<br>Leu        | tct<br>Ser        | gag<br>Glu        | gat<br>Asp<br>310 | cgg<br>Arg        | aga<br>Arg         | caa<br>G n        | gtg<br>Val        | act<br>Thr<br>315 | Arg               | gga<br>Gly        | tac<br>Tyr        | acc<br>Thr        | cag<br>Gln<br>320 | gag<br>Glu        | 1439 |
| aat<br>Asn        | cag<br>Gln        | gac<br>Asp        | aca<br>Thr<br>325 | tct<br>Ser        | tcc<br>Ser        | agg<br>Arg         | aga<br>Arg        | ttt<br>Phe<br>330 | act<br>Thr        | gcc<br>Ala        | ttc<br>Phe        | ccc<br>Pro        | tgt<br>Cys<br>335 | gtc<br>Val        | ttg<br>Leu        | 1487 |
| ggt<br>Gly        | tgt<br>Cys        | gaa<br>Glu<br>340 | ggc<br>Gly        | ttc<br>Phe        | acc<br>Thr        | tca<br>Ser         | gga<br>Gly<br>345 | Arg               | cgt<br>Arg        | tac<br>Tyr        | ttt<br>Phe        | gaa<br>Glu<br>350 | gtg<br>Val        | gat<br>Asp        | gtt<br>Val        | 1535 |
| ggc<br>Gly        | gaa<br>Glu        | gga<br>Gly        | acc<br>Thr        | gga<br>Gly        | tgg<br>Trp        | gat<br>Asp         | tta<br>Leu        | gga<br>Gly        | gtt<br>Val        | tgt<br>Cys        | atg<br>Met        | gaa<br>Glu        | aat<br>Asn        | gtg<br>Val        | cag<br>G n        | 1583 |



Met Cys Glu Gln Ala Leu Gly Lys Gly Cys Gly Ala Asp Ser Lys Lys 20 25 30

Lys Arg Pro Pro Gln Pro Pro Glu Glu Ser Gln Pro Pro Gln Ser Gln 35 40 45

Ala Gln Val Pro Pro Ala Ala Pro His His His His His Ser His 50 55 60

Ser Gly Pro Glu IIe Ser Arg IIe IIe Val Asp Pro Thr Thr Gly Lys 65 70 75 80

Arg Tyr Cys Arg Gly Lys Val Leu Gly Lys Gly Gly Phe Ala Lys Cys 85 90 95

Tyr Glu Met Thr Asp Leu Thr Asn Asn Lys Val Tyr Ala Ala Lys lle 100 105 110

| lle        | Pro        | His<br>115 | Ser        | Arg        |            | Ala        | Lys<br>120 | Pro        | His        | Gln        | Arg        | Glu<br>125 | Ц          | le         | Asp        |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| Lys        | Glu<br>130 | He         | Glu        | Leu        | His        | Arg<br>135 | Пе         | Leu        | His        | His        | Lys<br>140 | His        | Val        | Val        | Gln        |
| Phe<br>145 | Tyr        | His        | Tyr        | Phe        | Glu<br>150 | Asp        | Lys        | Glu        | Asn        | 11e<br>155 | Tyr        | He         | Leu        | Leu        | Glu<br>160 |
| Tyr        | Cys        | Ser        | Arg        | Arg<br>165 | Ser        | Met        | Ala        | His        | 11e<br>170 | Leu        | Lys        | Ala        | Arg        | Lys<br>175 | Val        |
| Leu        | Thr        | Glu        | Pro<br>180 | Glu        | Val        | Arg        | Tyr        | Tyr<br>185 | Leu        | Arg        | Gln        | He         | Val<br>190 | Ser        | Gly        |
| Leu        | Lys        | Tyr<br>195 | Leu        | His        | Glu        | Gln        | G u<br>200 | He         | Leu        | His        | Arg        | Asp<br>205 | Leu        | Lys        | Leu        |
| Gly        | Asn<br>210 | Phe        | Phe        | Пe         | Asn        | Glu<br>215 | Ala        | Met        | Glu        | Leu        | Lys<br>220 | Val        | Gly        | Asp        | Phe        |
| Gly<br>225 | Leu        | Ala        | Ala        | Arg        | Leu<br>230 | Glu        | Pro        | Leu        | Glu        | His<br>235 | Arg        | Arg        | Arg        | Thr        | lle<br>240 |
| Cys        | Gly        | Thr        | Pro        | Asn<br>245 | Tyr        | Leu        | Ser        | Pro        | Glu<br>250 | Val        | Leu        | Asn        | Lys        | Gln<br>255 | Gly        |
| His        | Gly        | Cys        | Glu<br>260 | Ser        | Asp        | lle        | Trp        | Ala<br>265 | Leu        | Gly        | Cys        | Val        | Met<br>270 | Tyr        | Thr        |
| Met        | Leu        | Leu<br>275 | Gly        | Arg        | Pro        | Pro        | Phe<br>280 | Glu        | Thr        | Thr        | Asn        | Leu<br>285 | Lys        | Glu        | Thr        |
| Tyr        | Arg<br>290 | Cys        | He         | Arg        | Glu        | Ala<br>295 | Arg        | Tyr        | Thr        | Met        | Pro<br>300 | Ser        | Ser        | Leu        | Leu        |
| Ala<br>305 |            | Ala        | Lys        | His        | Leu<br>310 | lle        | Ala        | Ser        | Met        | Leu<br>315 | Ser        | Lys        | Asn        | Pro        | Glu<br>320 |
| Asp        | Arg        | Pro        | Ser        | Leu<br>325 | Asp        | Asp        | lle        | He         | Arg<br>330 | His        | Asp        | Phe        | Phe        | Leu<br>335 | Gln        |
| Gly        | Phe        | Thr        | Pro<br>340 |            | Arg        | Leu        | Ser        | Ser<br>345 | Ser        | Cys        | Cys        | His        | Thr<br>350 | Val        | Pro        |
| Asp        | Phe        | His<br>355 |            | Ser        | Ser        | Pro        | Ala<br>360 | Lys        | Asn        | Phe        | Phe        | Lys<br>365 | Lys        | Ala        | Ala        |
| Ala        | Ala<br>370 |            | Phe        | Gly        | Gly        | Lys<br>375 | Lys        | Asp        | Lys        | Ala        | Arg<br>380 | Tyr        | lle        | Asp        | Thr        |
| His<br>385 |            | Arg        | , Val      | Ser        | Lys<br>390 | Glu        | ı Asp      | Glu        | Asp        | 11e<br>395 | Tyr        | Lys        | Leu        | Arg        | His<br>400 |
| Asp        | Leu        | ı Lys      | Lys        | Thr<br>405 |            | Πe         | . Thr      | Gin        | Gln<br>410 | Pro        | Ser        | Lys        | His        | Arg<br>415 | Thr        |
| Asp        | Glu        | ı Glu      | ı Lev      | ı Glr      | Pro        | Pro        | Thr        | Thr        | Thr        | Val        | Ala        | Arg        | ; Ser      | Gly        | Thr        |



Pro Ala Val Glu Asn Lys Gln Gln lle Gly Asp Ala lle Arg Met lle 435 440 445

Val Arg Gly Thr Leu Gly Ser Cys Ser Ser Ser Ser Glu Cys Leu Glu 450 455 460

Asp Ser Thr Met Gly Ser Val Ala Asp Thr Val Ala Arg Val Leu Arg 465 470 475 480

Gly Cys Leu Glu Asn Met Pro Glu Ala Asp Cys lle Pro Lys Glu Gln 485 490 495

Leu Ser Thr Ser Phe Gln Trp Val Thr Lys Trp Val Asp Tyr Ser Asn 500 505 510

Lys Tyr Gly Phe Gly Tyr Gln Leu Ser Asp His Thr Val Gly Val Leu 515 520 525

Phe Asn Asn Gly Ala His Met Ser Leu Leu Pro Asp Lys Lys Thr Val 530 540

His Tyr Tyr Ala Glu Leu Gly Gln Cys Ser Val Phe Pro Ala Thr Asp 545 550 555 560

Ala Pro Glu Gln Phe Ile Ser Gln Val Thr Val Leu Lys Tyr Phe Ser 565 570 575

His Tyr Met Glu Glu Asn Leu Met Asp Gly Gly Asp Leu Pro Ser Val 580 585 590

Thr Asp IIe Arg Arg Pro Arg Leu Tyr Leu Leu Gln Trp Leu Lys Ser 595 600 605

Asp Lys Ala Leu Met Met Leu Phe Asn Asp Gly Thr Phe Gln Val Asn 610 615 620

Phe Tyr His Asp His Thr Lys IIe IIe IIe Cys Ser Gln Asn Glu Glu 625 635 635

Tyr Leu Leu Thr Tyr lle Asn Glu Asp Arg lle Ser Thr Thr Phe Arg 645 650 655

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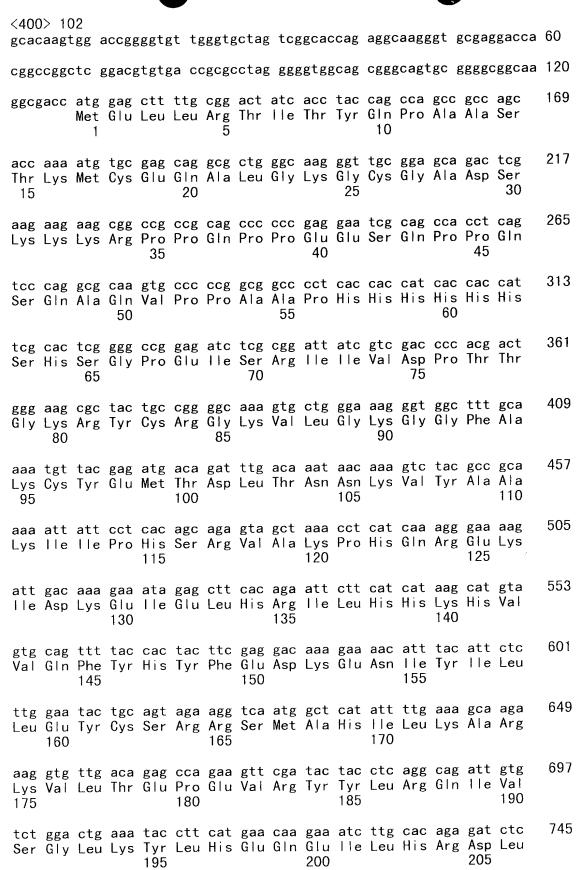
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|---|------------|
|   |            |
| gac ttc ggt ctg gca gcc agg cta gaa ccc ttg gaa cac aga agg agg<br>Asp Phe Gly Leu Ala Ala Arg Leu Glu Pro Leu Glu His Arg Arg Arg<br>225 230 235     | 5          |
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| caa gga cat ggc tgt gaa tca gac att tgg gcc ctg ggc tgt gta atg<br>Gln Gly His Gly Cys Glu Ser Asp lle Trp Ala Leu Gly Cys Val Met<br>255 260 265 270 | -          |
| tat aca atg tta cta ggg agg ccc cca ttt gaa act aca aat ctc aaa<br>Tyr Thr Met Leu Leu Gly Arg Pro Pro Phe Glu Thr Thr Asn Leu Lys<br>275 280 285     | a 985<br>s |
| gaa act tat agg tgc ata agg gaa gca agg tat aca atg ccg tcc tca<br>Glu Thr Tyr Arg Cys lle Arg Glu Ala Arg Tyr Thr Met Pro Ser Ser<br>290 295 300     | 1033       |
| ttg ctg gct cct gcc aag cac tta att gct agt atg ttg tcc aaa aac<br>Leu Leu Ala Pro Ala Lys His Leu IIe Ala Ser Met Leu Ser Lys Ass<br>305 310 315     | 1081<br>1  |
| cca gag gat cgt ccc agt ttg gat gac atc att cga cat gac ttt tt<br>Pro Glu Asp Arg Pro Ser Leu Asp Asp IIe IIe Arg His Asp Phe Phe<br>320 325 330      | 1129       |
| ttg cag ggc ttc act ccg gac aga ctg tct tct agc tgt tgt cat aca<br>Leu Gln Gly Phe Thr Pro Asp Arg Leu Ser Ser Ser Cys Cys His Thr<br>335 340 345 350 | •          |
| gtt cca gat ttc cac tta tca agc cca gct aag aat ttc ttt aag aag<br>Val Pro Asp Phe His Leu Ser Ser Pro Ala Lys Asn Phe Phe Lys Lys<br>355 360 365     | a 1225     |
| gca gct gct gct ctt ttt ggt ggc aaa aaa gac aaa gca aga tat at<br>Ala Ala Ala Leu Phe Gly Gly Lys Lys Asp Lys Ala Arg Tyr Ile<br>370 375 380          | 1273       |
| gac aca cat aat aga gtg tct aaa gaa gat gaa gac atc tac aag ct<br>Asp Thr His Asn Arg Val Ser Lys Glu Asp Glu Asp Ile Tyr Lys Lei<br>385 390 395      |            |
| agg cat gat ttg aaa aag act tca ata act cag caa ccc agc aaa cad<br>Arg His Asp Leu Lys Lys Thr Ser Ile Thr Gln Gln Pro Ser Lys His<br>400 405 410     | 1369       |
| agg aca gat gag gag ctc cag cca cct acc acc aca gtt gcc agg tc<br>Arg Thr Asp Glu Glu Leu Gln Pro Pro Thr Thr Thr Val Ala Arg Se<br>415 420 425 436   |            |
| gga aca ccc gca gta gaa aac aag cag cag att ggg gat gct att cg  | g 1465     |

| Gly               | Thr               | Pro               | Ala               | Va I<br>435       | J                 | Asn               | Lys               | Gln               | GIn<br>440        | lle               | Gly               | Asp               |                   | le<br>445         | Arg                   |      |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-----------------------|------|
| atg<br>Met        | ata<br>Ile        | gtc<br>Val        | aga<br>Arg<br>450 | ggg<br>Gly        | act<br>Thr        | ctt<br>Leu        | ggc<br>Gly        | agc<br>Ser<br>455 | tgt<br>Cys        | agc<br>Ser        | agc<br>Ser        | agc<br>Ser        | agt<br>Ser<br>460 | gaa<br>Glu        | tgc<br>Cys            | 1513 |
| ctt<br>Leu        | gaa<br>Glu        | gac<br>Asp<br>465 | agt<br>Ser        | acc<br>Thr        | atg<br>Met        | gga<br>Gly        | agt<br>Ser<br>470 | gtt<br>Val        | gca<br>Ala        | gac<br>Asp        | aca<br>Thr        | gtg<br>Val<br>475 | gca<br>Ala        | agg<br>Arg        | gtt<br>Val            | 1561 |
| ctt<br>Leu        | cgg<br>Arg<br>480 | gga<br>Gly        | tgt<br>Cys        | ctg<br>Leu        | gaa<br>Glu        | aac<br>Asn<br>485 | atg<br>Met        | ccg<br>Pro        | gaa<br>Glu        | gct<br>Ala        | gat<br>Asp<br>490 | tgc<br>Cys        | att<br>lle        | ccc<br>Pro        | aaa<br>Lys            | 1609 |
| gag<br>Glu<br>495 | cag<br>Gln        | ctg<br>Leu        | agc<br>Ser        | aca<br>Thr        | tca<br>Ser<br>500 | ttt<br>Phe        | cag<br>Gln        | tgg<br>Trp        | gtc<br>Val        | acc<br>Thr<br>505 | aaa<br>Lys        | tgg<br>Trp        | gtt<br>Val        | gat<br>Asp        | tac<br>Tyr<br>510     | 1657 |
| tct<br>Ser        | aac<br>Asn        | aaa<br>Lys        | tat<br>Tyr        | ggc<br>Gly<br>515 | ttt<br>Phe        | ggg<br>Gly        | tac<br>Tyr        | cag<br>Gln        | ctc<br>Leu<br>520 | tca<br>Ser        | gac<br>Asp        | cac<br>His        | acc<br>Thr        | gtc<br>Val<br>525 | ggt<br>Gly            | 1705 |
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| aca<br>Thr        | gtt<br>Val        | cac<br>His<br>545 | tat<br>Tyr        | tac<br>Tyr        | gca<br>Ala        | gag<br>Glu        | ctt<br>Leu<br>550 | ggc<br>Gly        | caa<br>Gln        | tgc<br>Cys        | tca<br>Ser        | gtt<br>Val<br>555 | ttc<br>Phe        | cca<br>Pro        | gca<br>Ala            | 1801 |
| aca<br>Thr        | gat<br>Asp<br>560 | Ala               | cct<br>Pro        | gag<br>Glu        | caa<br>Gln        | ttt<br>Phe<br>565 | att<br>Ile        | agt<br>Ser        | caa<br>Gln        | gtg<br>Val        | acg<br>Thr<br>570 | gtg<br>Val        | ctg<br>Leu        | aaa<br>Lys        | tac<br>Tyr            | 1849 |
| ttt<br>Phe<br>575 | Ser               | cat<br>His        | tac<br>Tyr        | atg<br>Met        | gag<br>Glu<br>580 | gag<br>Glu        | aac<br>Asn        | ctc<br>Leu        | atg<br>Met        | gat<br>Asp<br>585 | Gly               | gga<br>Gly        | gat<br>Asp        | ctg<br>Leu        | cct<br>Pro<br>590     | 1897 |
| agt<br>Ser        | gtt<br>Val        | act<br>Thr        | gat<br>Asp        | att<br>Ile<br>595 | cga<br>Arg        | aga<br>Arg        | cct<br>Pro        | cgg<br>Arg        | ctc<br>Leu<br>600 | lyr               | ctc<br>Leu        | ctt<br>Leu        | cag<br>Gln        | tgg<br>Trp<br>605 | cta<br>Leu            | 1945 |
| aaa<br>Lys        | tct<br>Ser        | gat<br>Asp        | aag<br>Lys<br>610 | A∤a               | cta<br>Leu        | atg<br>Met        | atg<br>Met        | ctc<br>Leu<br>615 | Phe               | aat<br>Asn        | gat<br>Asp        | ggc<br>Gly        | acc<br>Thr<br>620 | Phe               | cag<br>Gln            | 1993 |
| gtg<br>Val        | ; aat<br>Asn      | ttc<br>Phe<br>625 | Tyr               | cat<br>His        | gat<br>Asp        | cat<br>His        | aca<br>Thr<br>630 | Lys               | atc<br>   atc     | atc<br>   atc     | ato<br>He         | tgt<br>Cys<br>635 | Ser               | caa<br>Glr        | aat<br>Asn            | 2041 |
| gaa<br>Glu        | gaa<br>Glu<br>640 | ı Tyr             | ctt<br>Leu        | ctc<br>Leu        | acc<br>Thr        | tac<br>Tyr<br>645 | lle               | aat<br>Asr        | gag<br>Glu        | gat<br>Asp        | agg<br>Arg<br>650 | ; lle             | tct<br>Ser        | aca<br>Thr        | act<br>Thr            | 2089 |
| tto<br>Phe<br>655 | : Arg             | g ctg<br>g Leu    | ; aca<br>Thr      | act<br>Thr        | ctg<br>Leu<br>660 | ı Let             | g atg<br>ı Met    | tct<br>Ser        | ggc               | tgt<br>Cys<br>665 | s Ser             | tca<br>Ser        | gaa<br>Glu        | ı tta<br>ı Lei    | a aaa<br>u Lys<br>670 | 2137 |

2182

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Thr Gly Pro Asp Gly Lys Gly Met Asn Pro Pro Ser Tyr Tyr Thr Gln
50 55 60

Pro Ala Pro Ile Pro Asn Asn Asn Pro Ile Thr Val Gln Thr Val Tyr 65 70 75 80

Val Gln His Pro Ile Thr Phe Leu Asp Arg Pro Ile Gln Met Cys Cys 85 90 95

Pro Ser Cys Asn Lys Met Ile Val Ser Gln Leu Ser Tyr Asn Ala Gly 100 105 110

Ala Leu Thr Trp Leu Ser Cys Gly Ser Leu Cys Leu Leu Gly Cys Ile 115 120 125

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aag cgt ttg taggactcag ccagacgtgg agggagccgg gtgccgcagg 592 Lys Arg Leu 160

aagtcctttc cacctctcat ccagcttcac gcctggtgga ggttctgccc tggtggtctc 652 acctctccag ggggcccacc ttcatgtctt cttttggggg gaatacgtcg caaaactaac 712 aaatctccaa accccagaaa ttgctgcttg gagtcgtgca taggacttgc aaagacattc 772 cccttgagtg tcagttccac ggtttcctgc ctccctgaga ccctgagtcc tgccatctaa 832 ctgtgatcat tgccctatcc gaatatcttc ctgtgatctg ccatcagtgg ctctttttc 892 ctgcttccat gggcctttct ggtggcagtc tcaaactgag aagccacagt tgccttattt 952 ttgaggctgt tctgcccaga gctcggctga accagccttt agtgcctacc attatcttat 1012 tgagattctg taactgcaga cttcattagc acacagattc actttaattt cttaatttt 1132 tttttaaata caaggaggg gctattaaca cccagtacag acatatccac aaggtcgtaa 1192 atgcatgcta gaaaaatagg gctggatctt atcactgccc tgtctcccct tgtttctctg 1252 tgccagatct tcagtgcccc tttccataca gggatttttt tctcatagag taattatatg 1312 aacagttttt atgacctcct tttggtctga aatactttcg aacagaattt ctttttttta 1372 aaaaaaaaca gagatggggt cttactatgt tgcccaggct ggtgtcgaac tcctgggctc 1432 aagcgatcct tctgccttgg cctcccgaag tgctgggatt gcaggcataa gctaccatgc 1492 tgggcctgaa cataatttca agaggaggat ttataaaacc attttctgta atcaaatgat 1552 tggtgtcatt ttcccatttg ccaatgtagt ctcactt 1589

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<213> Homo sapiens

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Tyr Pro Thr Pro Pro Ala Pro Met Pro Gly Pro Thr Thr Gly Leu Val 35 40 45

| 50 55 GIV Met Ash Pro Pro Ser Tyr  | GIN           |            |
|--|---------------|------------|
| Pro Ala Pro Ile Pro Asn Asn Pro Ile Thr Val Gln Thr Val 65 70 75   | Tyr<br>80     |            |
| Val Gln His Pro lle Thr Phe Leu Asp Arg Pro Val Gln Met Cys<br>85 90 95  | Cys           |            |
| Pro Ser Cys Asn Lys Met Ile Val Ser Gln Leu Ser Tyr Asn Ala<br>100 105 110   | Gly           |            |
| Ala Leu Thr Trp Leu Ser Cys Gly Ser Leu Cys Leu Leu Gly Cys 115 120 125  | lle           |            |
| Ala Gly Cys Cys Phe lle Pro Phe Cys Val Asp Ala Leu Gln Asp 130 135 140  | Val           |            |
| Asp His Tyr Cys Pro Asn Cys Arg Ala Leu Leu Gly Thr Tyr Lys<br>145 150 155   | Arg<br>160    |            |
| Leu  |               |            |
| <210> 106<br><211> 1589<br><212> DNA<br><213> Homo sapiens   |               |            |
| <220><br><221> CDS<br><222> (70) (552)   |               |            |
| <400> 106 cctttctcg gggcgcccga aggccagctc agacctcccg gctcgacagg cggcg  | geggge 60     | )          |
| ggcggtaaa atg tcg gtt cca gga cct tac cag gcg gcc act ggg cc<br>Met Ser Val Pro Gly Pro Tyr Gln Ala Ala Thr Gly Pr<br>1 5 10           |               | 11         |
| tca gca cca tcc gca cct cca tcc tat gaa gag aca gtg gct gtt<br>Ser Ala Pro Ser Ala Pro Pro Ser Tyr Glu Glu Thr Val Ala Val<br>15 20 25 |               | 59         |
| agt tat tac ccc aca cct cca gct ccc atg cct ggg cca act acg<br>Ser Tyr Tyr Pro Thr Pro Pro Ala Pro Met Pro Gly Pro Thr Thr<br>35 40 45 |               | <b>)</b> 7 |
| ctt gtg acg ggg cct gat ggg aag ggc atg aat cct cct tcg tat<br>Leu Val Thr Gly Pro Asp Gly Lys Gly Met Asn Pro Pro Ser Tyr<br>50 55 60 | tat 25<br>Tyr | 55         |
| acc cag cca gcg ccc atc ccc aat aac aat cca att acc gtg cag Thr Gln Pro Ala Pro Ile Pro Asn Asn Pro Ile Thr Val Gln 65 70 75           |               | )3         |
| gtc tac gtg cag cac ccc atc acc ttt ttg gac cgc cct gtc caa  | atg 35        | 51         |

| Val              | Tyr<br>80         | Val               | Gln               | His               |                   | 11e<br>85  | Thr               | Phe               | Leu               | Asp               | Arg<br>90  | Pro               | ٧                 | ln                | Met               |      |
|------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------------|-------------------|-------------------|-------------------|-------------------|------------|-------------------|-------------------|-------------------|-------------------|------|
| tgt<br>Cys<br>95 | tgt<br>Cys        | cct<br>Pro        | tcc<br>Ser        | tgc<br>Cys        | aac<br>Asn<br>100 | aag<br>Lys | atg<br>Met        | atc<br>Ile        | gtg<br>Val        | agt<br>Ser<br>105 | cag<br>Gln | ctg<br>Leu        | tcc<br>Ser        | tat<br>Tyr        | aac<br>Asn<br>110 | 399  |
| gcc<br>Ala       | ggt<br>Gly        | gct<br>Ala        | ctg<br>Leu        | acc<br>Thr<br>115 | tgg<br>Trp        | ctg<br>Leu | tcc<br>Ser        | tgc<br>Cys        | ggg<br>Gly<br>120 | agc<br>Ser        | ctg<br>Leu | tgc<br>Cys        | ctg<br>Leu        | ctg<br>Leu<br>125 | ggg<br>Gly        | 447  |
| tgc<br>Cys       | ata<br>He         | gcg<br>Ala        | ggc<br>Gly<br>130 | Cys               | tgc<br>Cys        | ttc<br>Phe | atc<br>ile        | ccc<br>Pro<br>135 | ttc<br>Phe        | tgc<br>Cys        | gtg<br>Val | gat<br>Asp        | gcc<br>Ala<br>140 | ctg<br>Leu        | cag<br>Gln        | 495  |
| gac<br>Asp       | gtg<br>Val        | gac<br>Asp<br>145 | His               | tac<br>Tyr        | tgt<br>Cys        | ccc<br>Pro | aac<br>Asn<br>150 | tgc<br>Cys        | aga<br>Arg        | gct<br>Ala        | ctc<br>Leu | ctg<br>Leu<br>155 | ggc<br>Gly        | acc<br>Thr        | tac<br>Tyr        | 543  |
|                  | cgt<br>Arg<br>160 | Leu               |                   | gact              | cag               | ccag       | acgt              | gg a              | ggga              | gccg              | g gt       | gccg              | cagg              |                   |                   | 592  |
| aag              | tcct              | ttc               | сасс              | tctc              | at c              | cagc       | ttca              | c gc              | ctgg              | tgga              | ggt        | tctg              | ссс               | tggt              | ggtctc            | 652  |
| acc              | tctc              | cag               | gggg              | ссса              | cc t              | tcat       | gtct              | t ct              | tttg              | gggg              | gaa        | tacg              | tcg               | caaa              | actaac            | 712  |
| aaa              | tctc              | caa               | accc              | caga              | aa t              | tgct       | gctt              | g ga              | gtcg              | tgca              | tag        | gact              | tgc               | aaag              | acattc            | 772  |
|                  |                   |                   |                   |                   |                   |            |                   |                   |                   |                   |            |                   |                   |                   | atctaa            |      |
| ctg              | tgat              | cat               | tgcc              | ctat              | cc g              | aata       | tctt              | c ct              | gtga              | tctg              | cca        | tcag              | tgg               | ctct              | ttttc             | 892  |
|                  |                   |                   |                   |                   |                   |            |                   |                   |                   |                   |            |                   |                   |                   | ttattt            |      |
|                  |                   |                   |                   |                   |                   |            |                   |                   |                   |                   |            |                   |                   |                   | tcttat            |      |
|                  |                   |                   |                   |                   |                   |            |                   |                   |                   |                   |            |                   |                   |                   | tggctt            |      |
|                  |                   |                   |                   |                   |                   |            |                   |                   |                   |                   |            |                   |                   |                   | atttt             |      |
|                  |                   |                   |                   |                   |                   |            |                   |                   |                   |                   |            |                   |                   |                   | gtcgtaa           |      |
|                  |                   |                   |                   |                   |                   |            |                   |                   |                   |                   |            |                   |                   |                   | ttctctg           |      |
|                  |                   |                   |                   |                   |                   |            |                   |                   |                   |                   |            |                   |                   |                   | ttatatg           |      |
|                  |                   |                   |                   |                   |                   |            |                   |                   |                   |                   |            |                   |                   |                   | tttttt            |      |
|                  |                   |                   |                   |                   |                   |            |                   |                   |                   |                   |            |                   |                   |                   | tgggcto           |      |
|                  |                   |                   |                   |                   |                   |            |                   |                   |                   |                   |            |                   |                   |                   | accatgo           |      |
|                  |                   |                   |                   |                   |                   |            |                   |                   |                   |                   |            |                   |                   |                   | aaatga            |      |
|                  |                   |                   |                   |                   |                   |            |                   |                   | tcac <sup>.</sup> |                   |            |                   |                   |                   |                   | 1589 |

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<213> Homo sapiens

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Val Thr Thr Asn Leu Lys Leu Arg Asn Pro Ser Asp Arg Lys Val Cys 35 40 45

Phe Lys Val Lys Thr Thr Ala Pro Arg Arg Tyr Cys Val Arg Pro Asn 50 55 60

Ser Gly Ile Ile Asp Pro Gly Ser Thr Val Thr Val Ser Val Met Leu 65 70 75 80

Gln Pro Phe Asp Tyr Asp Pro Asn Glu Lys Ser Lys His Lys Phe Met 85 90 95

Val Gln Thr lle Phe Ala Pro Pro Asn Thr Ser Asp Met Glu Ala Val 100 105 110

Trp Lys Glu Ala Lys Pro Asp Glu Leu Met Asp Ser Lys Leu Arg Cys 115 120 125

Val Phe Glu Met Pro Asn Glu Asn Asp Lys Leu Asn Asp Met Glu Pro 130 135 140

Ser Lys Ala Val Pro Leu Asn Ala Ser Lys Gin Asp Gly Pro Met Pro 145 150 155 160

Lys Pro His Ser Val Ser Leu Asn Asp Thr Glu Thr Arg Lys Leu Met

Glu Glu Cys Lys Arg Leu Gln Gly Glu Met Met Lys Leu Ser Glu Glu 180 185 190

Asn Arg His Leu Arg Asp Glu Gly Leu Arg Leu Arg Lys Val Ala His 195 200 205

Ser Asp Lys Pro Gly Ser Thr Ser Thr Ala Ser Phe Arg Asp Asn Val 210 215 220

Thr Ser Pro Leu Pro Ser Leu Leu Val Val IIe Ala Ala IIe Phe IIe 225 230 235 240

Gly Phe Phe Leu Gly Lys Phe lle Leu 245

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765

cac agt gtt tca ctt aat gat acc gaa aca agg aaa cta atg gaa gag

His Ser Val Ser Led h Asp Thr Glu Thr Arg Lys Leu N tgt aaa aga ctt cag gga gaa atg atg aag cta tca gaa gaa aat cgg 813 Cys Lys Arg Leu Gln Gly Glu Met Met Lys Leu Ser Glu Glu Asn Arg cac ctg aga gat gaa ggt tta agg ctc aga aag gta gca cat tcg gat 861 His Leu Arg Asp Glu Gly Leu Arg Leu Arg Lys Val Ala His Ser Asp 205 200 909 aaa cct gga tca acc tca act gca tcc ttc aga gat aat gtc acc agt Lys Pro Gly Ser Thr Ser Thr Ala Ser Phe Arg Asp Asn Val Thr Ser 215 957 cct ctt cct tca ctt ctt gtt gta att gca gcc att ttc att gga ttc Pro Leu Pro Ser Leu Leu Val Val IIe Ala Ala IIe Phe IIe Gly Phe 235 240 230 ttt cta ggg aaa ttc atc ttg tagagtgaag catgcagagt gctgtttctt 1008 Phe Leu Gly Lys Phe Ile Leu 245 tttttttttt tctcttgacc agaaaaagat ttgtttacct accatttcat tggtagtatg 1068 gcccacggtg accatttttt tgtgtgtaca gcgtcatata ggctttgcct ttaatgatct 1128 cttacggtta gaaaacacaa taaaaacaaa ctgttcggct actggacagg ttgtatatta 1188 ccagatcatc actagcagat gtcagttgca cattgagtcc tttatgaaat tcataaataa 1248 . agaattgttc tttctttgtg gttttaataa gagttcaaga attgttcaga gtcttgtaaa 1308 tgttatttta ataatccctt taaattttat ctgttgctgt tacctcttga aatatgattt 1368 atttagattg ctaatcccac tcattcagga aatgccaaga ggtattcctt ggggaaatgg 1428 tgcctcttac agtgtaaatt tttcctcctt tacctttgct aatatcatgg cagaattttt 1488 cttatccctt gtgaggcagt tgttgactga gtttttcatc cttacaatcc tgtcccatgg 1548 1595 tatttaacat aaaaaaaat aaaactgtta acagattctt gctcgat <210> 109 <211> 540 <212> PRT <213> Homo sapiens

<400> 109

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Leu Arg Pro Glu His Phe Gln Glu Val Gly Tyr Ala Ala Pro Pro Ser 35

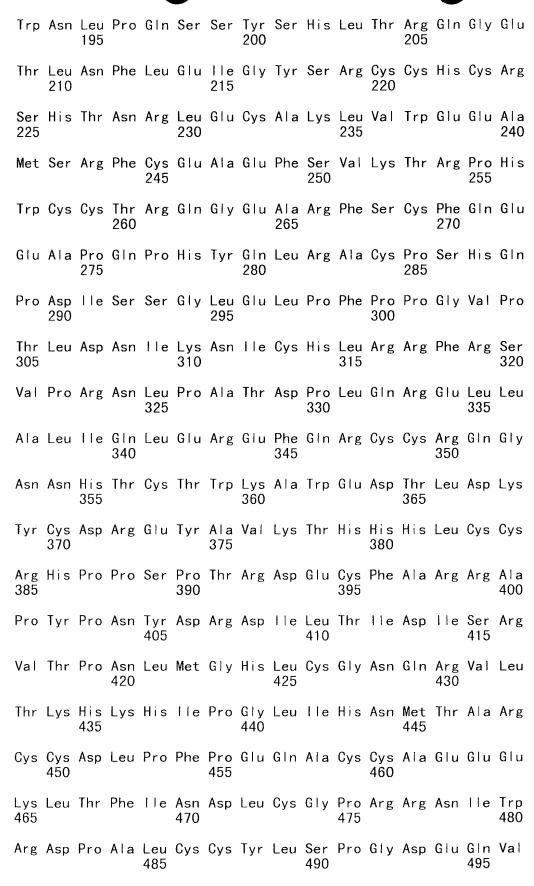
| Pro        | Pro<br>50  | Leu        | Ser        | Arg        | ser        | Leu<br>55  | Pro        | Met        | Asp        | His               | Pro<br>60  | Asp        | Ser        | Ser        | Gln        |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|------------|
| His<br>65  | Gly        | Pro        | Pro        | Phe        | Glu<br>70  | Gly        | Gln        | Ser        | Gln        | <b>Va</b> l<br>75 | G∣n        | Pro        | Pro        | Pro        | Ser<br>80  |
| Gln        | Glu        | Ala        | Thr        | Pro<br>85  | Leu        | Gln        | Gln        | Glu        | Lys<br>90  | Leu               | Leu        | Pro        | Ala        | Gln<br>95  | Leu        |
| Pro        | Ala        | Glu        | Lys<br>100 | Glu        | Val        | Gly        | Pro        | Pro<br>105 | Leu        | Pro               | Gln        | Glu        | Ala<br>110 | Val        | Pro        |
| Leu        | Gln        | Lys<br>115 | Glu        | Leu        | Pro        | Ser        | Leu<br>120 | Gln        | His        | Pro               | Asn        | Glu<br>125 | Gln        | Lys        | Glu        |
| Gly        | Thr<br>130 | Pro        | Ala        | Pro        | Phe        | Gly<br>135 | Asp        | Gln        | Ser        | His               | Pro<br>140 | Glu        | Pro        | Glu        | Ser        |
| Trp<br>145 | Asn        | Ala        | Ala        | Gln        | His<br>150 | Cys        | Gln        | Gln        | Asp        | Arg<br>155        | Ser        | Gln        | Gly        | Gly        | Trp<br>160 |
| Gly        | His        | Arg        | Leu        | Asp<br>165 | Gly        | Phe        | Pro        | Pro        | Gly<br>170 | Arg               | Pro        | Ser        | Pro        | Asp<br>175 | Asn        |
| Leu        | Asn        | Gln        | 11e<br>180 | Cys        | Leu        | Pro        | Asn        | Arg<br>185 | Gln        | His               | Val        | Val        | Tyr<br>190 | Gly        | Pro        |
| Trp        | Asn        | Leu<br>195 | Pro        | Gln        | Ser        | Ser        | Tyr<br>200 | Ser        | His        | Leu               | Thr        | Arg<br>205 | Gln        | Gly        | Glu        |
| Thr        | Leu<br>210 | Asn        | Phe        | Leu        | Glu        | 11e<br>215 | Gly        | Tyr        | Ser        | Arg               | Cys<br>220 | Cys        | His        | Cys        | Arg        |
| Ser<br>225 | His        | Thr        | Asn        | Arg        | Leu<br>230 | Glu        | Cys        | Ala        | Lys        | Leu<br>235        | Val        | Trp        | Glu        | Glu        | Ala<br>240 |
| Met        | Ser        | Arg        | Phe        | Cys<br>245 | Glu        | Ala        | Glu        | Phe        | Ser<br>250 | Val               | Lys        | Thr        | Arg        | Pro<br>255 | His        |
| Trp        | Cys        | Cys        | Thr<br>260 | Arg        | Gln        | Gly        | Glu        | Ala<br>265 | Arg        | Phe               | Ser        | Cys        | Phe<br>270 | Gln        | Glu        |
| Glu        | Ala        | Pro<br>275 | GIn        | Pro        | His        | Tyr        | G n<br>280 | Leu        | Arg        | Ala               | Cys        | Pro<br>285 | Ser        | His        | Gln        |
| Pro        | Asp<br>290 | lle        | Ser        | Ser        | Gly        | Leu<br>295 | Glu        | Leu        | Pro        | Phe               | Pro<br>300 | Pro        | Gly        | Val        | Pro        |
| Thr<br>305 | Leu        | Asp        | Asn        | Пe         | Lys<br>310 | Asn        | lle        | Cys        | His        | Leu<br>315        | Arg        | Arg        | Phe        | Arg        | Ser<br>320 |
| Val        | Pro        | Arg        | Asn        | Leu<br>325 | Pro        | Ala        | Thr        | Asp        | Pro<br>330 | Leu               | Gln        | Arg        | Glu        | Leu<br>335 | Leu        |
| Ala        | Leu        | He         | GIn<br>340 | Leu        | Glu        | Arg        | Glu        | Phe<br>345 | Gln        | Arg               | Cys        | Cys        | Arg<br>350 | Gln        | Gly        |

| Asn        | Asn                             | His<br>355 | Thr        | Cy.              | r          | Trp        | Lys<br>360 | Ala        | Trp              | Glu        | Asp        | Thr<br>365        |              | Asp              | Lys                   |     |
|------------|---------------------------------|------------|------------|------------------|------------|------------|------------|------------|------------------|------------|------------|-------------------|--------------|------------------|-----------------------|-----|
| Tyr        | Cys<br>370                      | Asp        | Arg        | Glu              | Tyr        | Ala<br>375 | Val        | Lys        | Thr              | His        | His<br>380 | His               | Leu          | Cys              | Cys                   |     |
| Arg<br>385 | His                             | Pro        | Pro        | Ser              | Pro<br>390 | Thr        | Arg        | Asp        | Glu              | Cys<br>395 | Phe        | Ala               | Arg          | Arg              | Ala<br>400            |     |
| Pro        | Tyr                             | Pro        | Asn        | Tyr<br>405       | Asp        | Arg        | Asp        | He         | Leu<br>410       | Thr        | lle        | Asp               | He           | Gly<br>415       | Arg                   |     |
| Val        | Thr                             | Pro        | Asn<br>420 | Leu              | Met        | Gly        | His        | Leu<br>425 | Cys              | Gly        | Asn        | Gln               | Arg<br>430   | Val              | Leu                   |     |
| Thr        | Lys                             | His<br>435 | Lys        | His              | lle        | Pro        | Gly<br>440 | Leu        | lle              | His        | Asn        | Met<br>445        | Thr          | Ala              | Arg                   |     |
| Cys        | Cys<br>450                      | Asp        | Leu        | Pro              | Phe        | Pro<br>455 | Glu        | Gln        | Ala              | Cys        | Cys<br>460 | Ala               | Glu          | Glu              | Glu                   |     |
| Lys<br>465 | Leu                             | Thr        | Phe        | lle              | Asn<br>470 | Asp        | Leu        | Cys        | Gly              | Pro<br>475 | Arg        | Arg               | Asn          | lle              | Trp<br>480            |     |
| Arg        | Asp                             | Pro        | Ala        | Leu<br>485       | Cys        | Cys        | Tyr        | Leu        | Ser<br>490       | Pro        | Gly        | Asp               | Glu          | Gln<br>495       | Val                   |     |
| Asn        | Cys                             | Phe        | Asn<br>500 | lle              | Asn        | Tyr        | Leu        | Arg<br>505 | Asn              | Val        | Ala        | Leu               | Val<br>510   | Ser              | Gly                   |     |
| Asp        | Thr                             | Glu<br>515 | Asn        | Ala              | Lys        | Gly        | Gln<br>520 | Gly        | Glu              | Gln        | Gly        | Ser<br>525        | Thr          | Gly              | Gly                   |     |
| Thr        | Asn<br>530                      | lle        | Ser        | Ser              | Thr        | Ser<br>535 | Glu        | Pro        | Lys              | Glu        | Glu<br>540 |                   |              |                  |                       |     |
| <21<br><21 | 0> 1<br>1> 18<br>2> DI<br>3> He | 810<br>NA  | sapi       | ens              |            |            |            |            |                  |            |            |                   |              |                  |                       |     |
|            | 1> C                            |            | (1         | 721)             |            |            |            |            |                  |            |            |                   |              |                  |                       |     |
|            | 0> 1<br>cgta                    |            | gcca       | ccag             | ac a       | agct       | tcag       | t gg       | ccgg             | ccct       | tca        | catc              | cag          | actt             | gcctga                | 60  |
| gag        | gacc                            | cac        | ctct       | gagt             | gt c       | cagt       | ggtc       | a gt       | tgcc             | ccag       | g a<br>M   | tg g<br>et G<br>1 | gg a<br>ly T | cc a<br>hr T     | ca gcc<br>hr Ala<br>5 | 116 |
| aga<br>Arg | gca<br>Ala                      | gcc<br>Ala | ttg<br>Leu | gtc<br>Val<br>10 | Leu        | acc<br>Thr | tat<br>Tyr | ttg<br>Leu | gct<br>Ala<br>15 | Val        | gct<br>Ala | tct<br>Ser        | gct<br>Ala   | gcc<br>Ala<br>20 | tct<br>Ser            | 164 |
| gag        | gga                             | ggr        | ttc        | acø              | gat        | aca        | gga        | Cap        | арр              | сая        | ctø        | agg               | сса          | gag              | cac                   | 212 |

| Glu               | Gly               | Gly               | Phe<br>25         | Th                | a                 | Thr               | Gly               | Gln<br>30         | Arg               | Gln               | Leu               | Arg               |                   | Glu               | His               |     |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-----|
| ttt<br>Phe        | caa<br>G n        | gaa<br>Glu<br>40  | gtt<br>Val        | ggc<br>Gly        | tac<br>Tyr        | gca<br>Ala        | gct<br>Ala<br>45  | ccc<br>Pro        | ccc<br>Pro        | tcc<br>Ser        | cca<br>Pro        | ccc<br>Pro<br>50  | cta<br>Leu        | tcc<br>Ser        | cga<br>Arg        | 260 |
| agc<br>Ser        | ctc<br>Leu<br>55  | ccc<br>Pro        | atg<br>Met        | gat<br>Asp        | cac<br>His        | cct<br>Pro<br>60  | gac<br>Asp        | tcc<br>Ser        | tct<br>Ser        | cag<br>Gln        | cat<br>His<br>65  | ggc<br>Gly        | cct<br>Pro        | ccc<br>Pro        | ttt<br>Phe        | 308 |
| gag<br>Glu<br>70  | gga<br>Gly        | cag<br>Gln        | agt<br>Ser        | caa<br>G n        | gtg<br>Val<br>75  | cag<br>Gln        | ccc<br>Pro        | cct<br>Pro        | ccc<br>Pro        | tct<br>Ser<br>80  | cag<br>Gln        | gag<br>Glu        | gcc<br>Ala        | acc<br>Thr        | cct<br>Pro<br>85  | 356 |
| ctc<br>Leu        | caa<br>Gln        | cag<br>Gln        | gaa<br>Glu        | aag<br>Lys<br>90  | ctg<br>Leu        | cta<br>Leu        | cct<br>Pro        | gcc<br>Ala        | caa<br>Gln<br>95  | ctc<br>Leu        | cct<br>Pro        | gct<br>Ala        | gaa<br>Glu        | aag<br>Lys<br>100 | gaa<br>Glu        | 404 |
| gtg<br>Val        | ggt<br>Gly        | ccc<br>Pro        | cct<br>Pro<br>105 | ctc<br>Leu        | cct<br>Pro        | cag<br>Gln        | gaa<br>Glu        | gct<br>Ala<br>110 | gtc<br>Val        | ccc<br>Pro        | ctc<br>Leu        | caa<br>Gln        | aaa<br>Lys<br>115 | gag<br>Glu        | ctg<br>Leu        | 452 |
| ccc<br>Pro        | tct<br>Ser        | ctc<br>Leu<br>120 | cag<br>Gln        | cac<br>His        | ccc<br>Pro        | aat<br>Asn        | gaa<br>Glu<br>125 | cag<br>Gln        | aag<br>Lys        | gaa<br>Glu        | gga<br>Gly        | acg<br>Thr<br>130 | cca<br>Pro        | gct<br>Ala        | cca<br>Pro        | 500 |
| ttt<br>Phe        | ggg<br>Gly<br>135 | gac<br>Asp        | cag<br>G n        | agc<br>Ser        | cat<br>His        | cca<br>Pro<br>140 | gaa<br>Glu        | cct<br>Pro        | gag<br>Glu        | tcc<br>Ser        | tgg<br>Trp<br>145 | aat<br>Asn        | gca<br>Ala        | gcc<br>Ala        | cag<br>Gln        | 548 |
| cac<br>His<br>150 | tgc<br>Cys        | caa<br>Gln        | cag<br>Gln        | gac<br>Asp        | cgg<br>Arg<br>155 | tcc<br>Ser        | caa<br>Gln        | ggg<br>Gly        | ggc<br>Gly        | tgg<br>Trp<br>160 | ggc<br>Gly        | cac<br>His        | cgg<br>Arg        | ctg<br>Leu        | gat<br>Asp<br>165 | 596 |
| ggc<br>Gly        | ttc<br>Phe        | ccc<br>Pro        | cct<br>Pro        | ggg<br>Gly<br>170 | cgg<br>Arg        | cct<br>Pro        | tct<br>Ser        | cca<br>Pro        | gac<br>Asp<br>175 | aat<br>Asn        | ctg<br>Leu        | aac<br>Asn        | caa<br>Gln        | atc<br>  e<br>180 | tgc<br>Cys        | 644 |
| ctt<br>Leu        | cct<br>Pro        | aac<br>Asn        | cgt<br>Arg<br>185 | cag<br>Gln        | cat<br>His        | gtg<br>Val        | gta<br>Val        | tat<br>Tyr<br>190 | ggt<br>Gly        | ccc<br>Pro        | tgg<br>Trp        | aac<br>Asn        | cta<br>Leu<br>195 | cca<br>Pro        | cag<br>Gln        | 692 |
| tcc<br>Ser        | agc<br>Ser        | tac<br>Tyr<br>200 | Ser               | cac<br>His        | ctc<br>Leu        | act<br>Thr        | cgc<br>Arg<br>205 | cag<br>Gln        | ggt<br>Gly        | gag<br>Glu        | acc<br>Thr        | ctc<br>Leu<br>210 | aat<br>Asn        | ttc<br>Phe        | ctg<br>Leu        | 740 |
| gag<br>G u        | att<br>Ile<br>215 | gga<br>Gly        | tat<br>Tyr        | tcc<br>Ser        | cgc<br>Arg        | tgc<br>Cys<br>220 | tgc<br>Cys        | cac<br>His        | tgc<br>Cys        | cgc<br>Arg        | agc<br>Ser<br>225 | cac<br>His        | aca<br>Thr        | aac<br>Asn        | cgc<br>Arg        | 788 |
| cta<br>Leu<br>230 | gag<br>Glu        | tgt<br>Cys        | gcc<br>Ala        | aaa<br>Lys        | ctt<br>Leu<br>235 | gtg<br>Val        | tgg<br>Trp        | gag<br>Glu        | gaa<br>Glu        | gca<br>Ala<br>240 | Met               | agc<br>Ser        | cga<br>Arg        | ttc<br>Phe        | tgt<br>Cys<br>245 | 836 |
| gag<br>G u        | gcc<br>Ala        | gag<br>G u        | ttc<br>Phe        | tcg<br>Ser<br>250 | gtc<br>Val        | aag<br>Lys        | acc<br>Thr        | cga<br>Arg        | ccc<br>Pro<br>255 | His               | tgg<br>Trp        | tgc<br>Cys        | tgc<br>Cys        | acg<br>Thr<br>260 | cgg<br>Arg        | 884 |

| ca<br>Gl          | g ggg<br>n Gly        | g gag<br>y Glu      | gct<br>Ala<br>265 | ı Arg             | tto<br>Phe        | tcc<br>Ser        | tgc<br>Cys        | ttc<br>Phe<br>270 | Gln               | gag<br>Glu        | gaa<br>Glu        | gct<br>Ala        | ccc<br>Pro<br>275 | Gln               | cca<br>Pro        | 932  |
|-------------------|-----------------------|---------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| ca<br>Hi          | c tad<br>s Tyr        | c cag<br>Gln<br>280 | Leu               | cgg<br>Arg        | gcc               | tgc<br>Cys        | Pro<br>285        | Ser               | cat<br>His        | cag<br>Gln        | cct<br>Pro        | gat<br>Asp<br>290 | He                | tcc<br>Ser        | tcg<br>Ser        | 980  |
| gg<br>G           | t ctt<br>y Lei<br>295 | gag<br>Glu          | ctg<br>Leu        | cct<br>Pro        | ttc<br>Phe        | cct<br>Pro<br>300 | Pro               | ggg<br>G y        | gtg<br>Val        | ccc<br>Pro        | aca<br>Thr<br>305 | Leu               | gac<br>Asp        | aat<br>Asn        | atc<br>Ile        | 1028 |
| aa<br>Ly<br>31    | s Asr                 | atc<br>Ille         | tgc<br>Cys        | cac<br>His        | ctg<br>Leu<br>315 | Arg               | cgc<br>Arg        | ttc<br>Phe        | cgc<br>Arg        | tct<br>Ser<br>320 | gtg<br>Val        | cca<br>Pro        | cgc<br>Arg        | aac<br>Asn        | ctg<br>Leu<br>325 | 1076 |
| ec.<br>Pr         | a gct<br>o Ala        | act<br>Thr          | gac<br>Asp        | ccc<br>Pro<br>330 | cta<br>Leu        | caa<br>Gln        | agg<br>Arg        | gag<br>Glu        | ctg<br>Leu<br>335 | ctg<br>Leu        | gca<br>Ala        | ctg<br>Leu        | atc<br>lle        | cag<br>Gln<br>340 | ctg<br>Leu        | 1124 |
| ga;<br>Gli        | g agg<br>u Arg        | gag<br>Glu          | ttc<br>Phe<br>345 | cag<br>Gln        | cgc<br>Arg        | tgc<br>Cys        | tgc<br>Cys        | cgc<br>Arg<br>350 | cag<br>Gln        | ggg<br>Gly        | aac<br>Asn        | aat<br>Asn        | cac<br>His<br>355 | acc<br>Thr        | tgt<br>Cys        | 1172 |
| aca<br>Thi        | a tgg<br>r Trp        | aag<br>Lys<br>360   | gcc<br>Ala        | tgg<br>Trp        | gag<br>Glu        | gat<br>Asp        | acc<br>Thr<br>365 | ctt<br>Leu        | gac<br>Asp        | aaa<br>Lys        | tac<br>Tyr        | tgt<br>Cys<br>370 | gac<br>Asp        | cgg<br>Arg        | gag<br>Glu        | 1220 |
| ta:<br>Ty:        | gct<br>Ala<br>375     | gtg<br>Val          | aag<br>Lys        | acc<br>Thr        | cac<br>His        | cac<br>His<br>380 | cac<br>His        | ttg<br>Leu        | tgt<br>Cys        | tgc<br>Cys        | cgc<br>Arg<br>385 | cac<br>His        | cct<br>Pro        | ccc<br>Pro        | agc<br>Ser        | 1268 |
| cct<br>Pro<br>390 | Thr                   | cgg<br>Arg          | gat<br>Asp        | gag<br>Glu        | tgc<br>Cys<br>395 | ttt<br>Phe        | gcc<br>Ala        | cgt<br>Arg        | cgg<br>Arg        | gct<br>Ala<br>400 | cct<br>Pro        | tac<br>Tyr        | ccc<br>Pro        | aac<br>Asn        | tat<br>Tyr<br>405 | 1316 |
| gac<br>Asp        | cgg<br>Arg            | gac<br>Asp          | He                | Leu               | acc<br>Thr        | Пe                | Asp               | lle               | Gly               | Arg               | Va∣               | Thr               | Pro               | aac<br>Asn<br>420 | ctc<br>Leu        | 1364 |
|                   |                       | cac<br>His          |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | 1412 |
| att<br>He         | cct<br>Pro            | ggg<br>Gly<br>440   | ctg<br>Leu        | atc<br>lle        | cac<br>His        | aac<br>Asn        | atg<br>Met<br>445 | act<br>Thr        | gcc<br>Ala        | cgc<br>Arg        | tgc<br>Cys        | tgt<br>Cys<br>450 | gac<br>Asp        | ctg<br>Leu        | cca<br>Pro        | 1460 |
| ttt<br>Phe        | cca<br>Pro<br>455     | gaa<br>Glu          | cag<br>Gln        | gcc<br>Ala        | tgc<br>Cys        | tgt<br>Cys<br>460 | gca<br>Ala        | gag<br>Glu        | gag<br>Glu        | Glu               | aaa<br>Lys<br>465 | tta<br>Leu        | acc<br>Thr        | ttc<br>Phe        | atc<br>lle        | 1508 |
| aat<br>Asn<br>470 | gat<br>Asp            | ctg<br>Leu          | tgt<br>Cys        | Gly               | ccc<br>Pro<br>475 | cga<br>Arg        | cgt<br>Arg        | aac<br>Asn        | He                | tgg<br>Trp<br>480 | cga<br>Arg        | gac<br>Asp        | cct<br>Pro        | Ala               | ctc<br>Leu<br>485 | 1556 |
| tgc               | tgt                   | tac                 | ctg               | agt               | cct               | ggg               | gat               | gaa               | cag               | gtc               | aac               | tgc               | ttc               | aac               | atc               | 1604 |

| Cys   | Cys  | Tyr               | Leu               | Ser<br>490 |            | Gly        | Asp               | Glu               | GIn<br>495 | Val        | Asn        | Cys               | F                 | Asn<br>500 | lle        |      |
|---|--|-------------------|-------------------|------------|------------|------------|-------------------|-------------------|------------|------------|------------|-------------------|-------------------|------------|------------|------|
| aat<br>Asn  | tat<br>Tyr   | ctg<br>Leu        | agg<br>Arg<br>505 | aac<br>Asn | gtg<br>Val | gct<br>Ala | cta<br>Leu        | gtg<br>Val<br>510 | tct<br>Ser | gga<br>Gly | gac<br>Asp | act<br>Thr        | gag<br>Glu<br>515 | aac<br>Asn | gcc<br>Ala | 1652 |
| aag<br>Lys  | ggc<br>Gly   | cag<br>Gln<br>520 | ggg<br>Gly        | gag<br>Glu | cag<br>Gln | ggc<br>Gly | tca<br>Ser<br>525 | act<br>Thr        | gga<br>Gly | gga<br>Gly | aca<br>Thr | aat<br>Asn<br>530 | atc<br>  e        | agc<br>Ser | tcc<br>Ser | 1700 |
|   | tct<br>Ser<br>535  |                   |                   |            |            |            | tga               | gtcad             | ccc (      | caga       | gccct      | ta ga             | agggt             | tcaga      | а          | 1751 |
| tggg  | tggggggaac cccaccctgc cccacccatc tgaacactca ttacactaaa cacctcttg |                   |                   |            |            |            |                   |                   |            |            |            |                   |                   |            |            | 1810 |
| <210> 111<br><211> 540<br><212> PRT<br><213> Homo sapiens |  |                   |                   |            |            |            |                   |                   |            |            |            |                   |                   |            |            |      |
|   | O> 11<br>Gly   |                   | Thr               | Ala<br>5   | Arg        | Ala        | Ala               | Leu               | Val<br>10  | Leu        | Thr        | Tyr               | Leu               | Ala<br>15  | Val        |      |
| Ala   | Ser  | Ala               | Ala<br>20         | Ser        | Glu        | Gly        | Gly               | Phe<br>25         | Thr        | Ala        | Thr        | Gly               | GIn<br>30         | Arg        | Gin        |      |
| Leu   | Arg  | Pro<br>35         | Glu               | His        | Phe        | Gln        | Glu<br>40         | Val               | Gly        | Tyr        | Ala        | Ala<br>45         | Pro               | Pro        | Ser        |      |
| Pro   | Pro<br>50  | Leu               | Ser               | Arg        | Ser        | Leu<br>55  | Pro               | Met               | Asp        | His        | Pro<br>60  | Asp               | Ser               | Ser        | Gln        |      |
| His<br>65   | Gly  | Pro               | Pro               | Phe        | Glu<br>70  | Gly        | Gln               | Ser               | Gln        | Va l<br>75 | Gin        | Pro               | Pro               | Pro        | Ser<br>80  |      |
| Gln   | Glu  | Ala               | Thr               | Pro<br>85  | Leu        | Gln        | Gln               | Glu               | Lys<br>90  | Leu        | Leu        | Pro               | Ala               | Gln<br>95  | Leu        |      |
| Pro   | Ala  | Glu               | Lys<br>100        | Glu        | Val        | Gly        | Pro               | Pro<br>105        | Leu        | Pro        | Gln        | Glu               | Ala<br>110        | Val        | Pro        |      |
| Leu   | Gln  | Lys<br>115        | Glu               | Leu        | Pro        | Ser        | Leu<br>120        | Gln               | His        | Pro        | Asn        | Glu<br>125        | Gln               | Lys        | Glu        |      |
| Gly   | Thr<br>130   | Pro               | Ala               | Pro        | Phe        | Gly<br>135 | Asp               | Gln               | Ser        | His        | Pro<br>140 | Glu               | Pro               | Glu        | Ser        |      |
| Trp<br>145  | Asn  | Ala               | Ala               | Gln        | His<br>150 | Cys        | Gln               | Gln               | Asp        | Arg<br>155 | Ser        | Gln               | Gly               | Gly        | Trp<br>160 |      |
| Gly   | His  | Arg               | Leu               | Asp<br>165 | Gly        | Phe        | Pro               | Pro               | Gly<br>170 | Arg        | Pro        | Ser               | Pro               | Asp<br>175 | Asn        |      |
| ييم ا   | Aen  | Gla               | ماا               | Cve        | ينما       | Pro        | Aen               | Ara               | Gln        | Hie        | Val        | Val               | Tyr               | Glv        | Pro        |      |

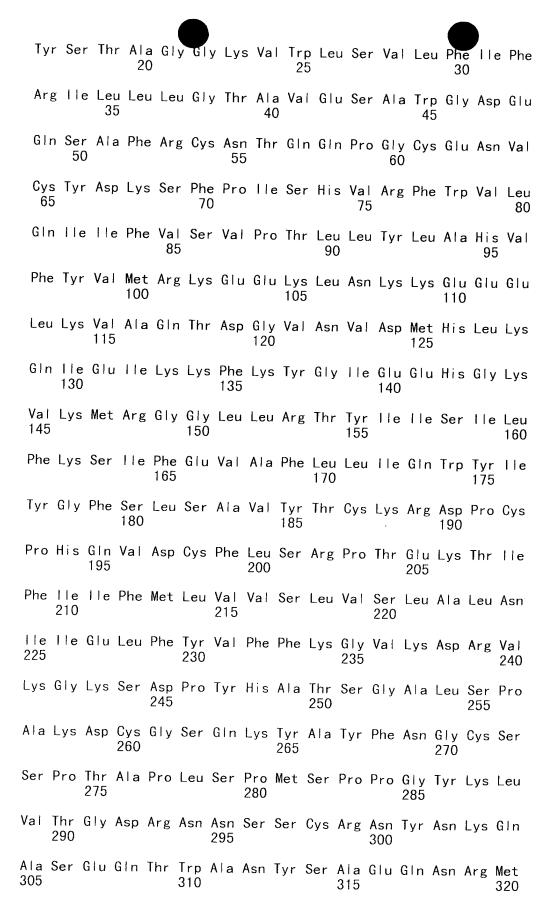


Asn Cys Phe Asn Ile Asn Tyr Leu Arg Asn Val Ala Leu Val Ser Gly 505 Asp Thr Glu Asn Ala Lys Gly Gln Gly Glu Gln Gly Ser Thr Gly Gly 520 Thr Asn lle Ser Ser Thr Ser Glu Pro Lys Glu Glu 535 <210> 112 <211> 1810 <212> DNA <213> Homo sapiens <220> <221> CDS <222> (102).. (1721) <400> 112 aaccgtaaca gccaccagac aagcttcagt ggccggccct tcacatccag acttgcctga 60 gaggacccac ctctgagtgt ccagtggtca gttgccccag g atg ggg acc aca gcc 116 Met Gly Thr Thr Ala 5 1 164 aga gca gcc ttg gtc ttg acc tat ttg gct gtt gct tct gcc tct Arg Ala Ala Leu Val Leu Thr Tyr Leu Ala Val Ala Ser Ala Ala Ser 212 gag gga ggc ttc acg gct aca gga cag agg cag ctg agg cca gag cac Glu Gly Gly Phe Thr Ala Thr Gly Gln Arg Gln Leu Arg Pro Glu His 260 ttt caa gaa gtt ggc tac gca gct ccc ccc tcc cca ccc cta tcc cga Phe Gln Glu Val Gly Tyr Ala Ala Pro Pro Ser Pro Pro Leu Ser Arg 45 40 308 ago ctc ccc atg gat cac cct gac tcc tct cag cat ggc cct ccc ttt Ser Leu Pro Met Asp His Pro Asp Ser Ser Gln His Gly Pro Pro Phe 55 gag gga cag agt caa gtg cag ccc cct ccc tct cag gag gcc acc cct 356 Glu Gly Gln Ser Gln Val Gln Pro Pro Pro Ser Gln Glu Ala Thr Pro 70 404 ctc caa cag gaa aag ctg cta cct gcc caa ctc cct gct gaa aag gaa Leu Gln Gln Glu Lys Leu Leu Pro Ala Gln Leu Pro Ala Glu Lys Glu 100 90 452 gtg ggt ccc cct ctc cct cag gaa gct gtc ccc ctc caa aaa gag ctg Val Gly Pro Pro Leu Pro Gln Glu Ala Val Pro Leu Gln Lys Glu Leu 110 500 ccc tct ctc cag cac ccc aat gaa cag aag gaa gga acg cca gct cca Pro Ser Leu Gln His Pro Asn Glu Gln Lys Glu Gly Thr Pro Ala Pro

120

|   | ttt<br>Phe        | ggg<br>Gly<br>135 | Asp               | cag<br>Gln        | agc<br>Ser        | cat<br>His        | cca<br>Pro<br>140 | Glu               | cct<br>Pro        | gag<br>Glu        | tcc<br>Ser        | tgg<br>Trp<br>145 | aat<br>Asn        | gca<br>Ala        | gcc<br>Ala        | cag<br>Gln        | 548  |
|---|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
|   | cac<br>His<br>150 | Cys               | caa<br>Gln        | cag<br>Gln        | gac<br>Asp        | cgg<br>Arg<br>155 | Ser               | caa<br>Gln        | ggg<br>Gly        | ggc<br>Gly        | tgg<br>Trp<br>160 | Gly               | cac<br>His        | cgg<br>Arg        | ctg<br>Leu        | gat<br>Asp<br>165 | 596  |
|   | ggc<br>Gly        | ttc<br>Phe        | ccc<br>Pro        | cct<br>Pro        | ggg<br>Gly<br>170 | cgg<br>Arg        | cct<br>Pro        | tct<br>Ser        | cca<br>Pro        | gac<br>Asp<br>175 | aat<br>Asn        | ctg<br>Leu        | aac<br>Asn        | caa<br>Gln        | atc<br>IIe<br>180 | Cys               | 644  |
|   | ctt<br>Leu        | cct<br>Pro        | aac<br>Asn        | cgt<br>Arg<br>185 | cag<br>Gln        | cat<br>His        | gtg<br>Val        | gta<br>Val        | tat<br>Tyr<br>190 | ggt<br>Gly        | ccc<br>Pro        | tgg<br>Trp        | aac<br>Asn        | cta<br>Leu<br>195 | cca<br>Pro        | cag<br>G n        | 692  |
|   | tcc<br>Ser        | agc<br>Ser        | tac<br>Tyr<br>200 | tcc<br>Ser        | cac<br>His        | ctc<br>Leu        | act<br>Thr        | cgc<br>Arg<br>205 | cag<br>Gln        | ggt<br>Gly        | gag<br>Glu        | acc<br>Thr        | ctc<br>Leu<br>210 | aat<br>Asn        | ttc<br>Phe        | ctg<br>Leu        | 740  |
|   | gag<br>Glu        | att<br>lle<br>215 | gga<br>Gly        | tat<br>Tyr        | tcc<br>Ser        | cgc<br>Arg        | tgc<br>Cys<br>220 | tgc<br>Cys        | cac<br>His        | tgc<br>Cys        | cgc<br>Arg        | agc<br>Ser<br>225 | cac<br>His        | aca<br>Thr        | aac<br>Asn        | cgc<br>Arg        | 788  |
|   |                   |                   |                   |                   |                   | ctt<br>Leu<br>235 |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | 836  |
| ( | gag<br>Glu        | gcc<br>Ala        | gag<br>Glu        | ttc<br>Phe        | tcg<br>Ser<br>250 | gtc<br>Val        | aag<br>Lys        | acc<br>Thr        | cga<br>Arg        | ccc<br>Pro<br>255 | cac<br>His        | tgg<br>Trp        | tgc<br>Cys        | tgc<br>Cys        | acg<br>Thr<br>260 | cgg<br>Arg        | 884  |
| ( | cag<br>Gln        | ggg<br>Gly        | gag<br>Glu        | gct<br>Ala<br>265 | cgg<br>Arg        | ttc<br>Phe        | tcc<br>Ser        | tgc<br>Cys        | ttc<br>Phe<br>270 | cag<br>Gln        | gag<br>Glu        | gaa<br>Glu        | gct<br>Ala        | ccc<br>Pro<br>275 | cag<br>G¦n        | cca<br>Pro        | 932  |
| } | ac<br>lis         | tac<br>Tyr        | cag<br>G n<br>280 | ctc<br>Leu        | cgg<br>Arg        | gcc<br>Ala        | tgc<br>Cys        | ccc<br>Pro<br>285 | agc<br>Ser        | cat<br>His        | cag<br>Gln        | cct<br>Pro        | gat<br>Asp<br>290 | att<br>He         | tcc<br>Ser        | tcg<br>Ser        | 980  |
| ( | Зlу               | ctt<br>Leu<br>295 | gag<br>Glu        | ctg<br>Leu        | cct<br>Pro        | ttc<br>Phe        | cct<br>Pro<br>300 | cct<br>Pro        | ggg<br>Gly        | gtg<br>Val        | ccc<br>Pro        | aca<br>Thr<br>305 | ttg<br>Leu        | gac<br>Asp        | aat<br>Asn        | atc<br>He         | 1028 |
| L |                   |                   |                   |                   |                   | ctg<br>Leu<br>315 |                   |                   |                   |                   |                   |                   |                   |                   |                   | ctg<br>Leu<br>325 | 1076 |
| F | ca<br>ro          | gct<br>Ala        | act<br>Thr        | gac<br>Asp        | ccc<br>Pro<br>330 | cta<br>Leu        | caa<br>Gln        | agg<br>Arg        | Glu               | ctg<br>Leu<br>335 | ctg<br>Leu        | gca<br>Ala        | ctg<br>Leu        | atc<br>Ile        | cag<br>Gln<br>340 | ctg<br>Leu        | 1124 |
| g | ag<br>Hu          | agg<br>Arg        | Glu               | ttc<br>Phe<br>345 | cag<br>Gln        | cgc<br>Arg        | tgc<br>Cys        | Cys               | cgc<br>Arg<br>350 | cag<br>Gln        | ggg<br>Gly        | aac<br>Asn        | Asn               | cac<br>His<br>355 | acc<br>Thr        | tgt<br>Cys        | 1172 |
| а | са                | tgg               | aag               | gcc               | tgg               | gag               | gat               | acc               | ctt               | gac               | aaa               | tac               | tgt               | gac               | cgg               | gag               | 1220 |

| Thr  | Trp        | Lys<br>360        | Ala               | Tr         | u          | Asp               | Thr<br>365        | Leu               | Asp        | Lys        | Tyr        | Cys<br>370        |                   | Arg        | Glu        |      |
|--|------------|-------------------|-------------------|------------|------------|-------------------|-------------------|-------------------|------------|------------|------------|-------------------|-------------------|------------|------------|------|
|  |            |                   |                   |            |            | cac<br>His<br>380 |                   |                   |            |            |            |                   |                   |            |            | 1268 |
|  |            |                   |                   |            |            | ttt<br>Phe        |                   |                   |            |            |            |                   |                   |            |            | 1316 |
|  |            |                   |                   |            |            | att<br>He         |                   |                   |            |            |            |                   |                   |            |            | 1364 |
|  |            |                   |                   |            |            | aac<br>Asn        |                   |                   |            |            |            |                   |                   |            |            | 1412 |
|  |            |                   |                   |            |            | aac<br>Asn        |                   |                   |            |            |            |                   |                   |            |            | 1460 |
|  |            |                   |                   |            |            | tgt<br>Cys<br>460 |                   |                   |            |            |            |                   |                   |            |            | 1508 |
|  |            |                   |                   |            |            | cga<br>Arg        |                   |                   |            |            |            |                   |                   |            |            | 1556 |
|  |            |                   |                   |            |            | ggg<br>Gly        |                   |                   |            |            |            |                   |                   |            |            | 1604 |
| aat<br>Asn   | tat<br>Tyr | ctg<br>Leu        | agg<br>Arg<br>505 | aac<br>Asn | gtg<br>Val | gct<br>Ala        | cta<br>Leu        | gtg<br>Val<br>510 | tct<br>Ser | gga<br>Gly | gac<br>Asp | act<br>Thr        | gag<br>Glu<br>515 | aac<br>Asn | gcc<br>Ala | 1652 |
| aag<br>Lys   | ggc<br>Gly | cag<br>Gln<br>520 | ggg<br>Gly        | gag<br>Glu | cag<br>Gln | ggc<br>Gly        | tca<br>Ser<br>525 | act<br>Thr        | gga<br>Gly | gga<br>Gly | aca<br>Thr | aat<br>Asn<br>530 | atc<br>He         | agc<br>Ser | tcc<br>Ser | 1700 |
|  |            |                   | ccc<br>Pro        |            |            | gaa<br>Glu<br>540 | tgag              | gtcac             | cc c       | agag       | gccct      | a ga              | agggt             | caga       | 3          | 1751 |
| tggggggaac cccaccctgc cccacccatc tgaacactca ttacactaaa cacctcttg |            |                   |                   |            |            |                   |                   |                   |            |            |            |                   |                   | 1810       |            |      |
| <210> 113<br><211> 382<br><212> PRT<br><213> Homo sapiens        |            |                   |                   |            |            |                   |                   |                   |            |            |            |                   |                   |            |            |      |
| <400<br>Met<br>1   |            |                   | Trp               | Ser<br>5   | Ala        | Leu               | G∣y               | Lys               | Leu<br>10  | Leu        | Asp        | Lys               | Val               | G n<br>15  | Ala        |      |



|  |              |              |                  |                  | _                |            |            |                  |                  |            |            |            |                  |                  |            |     |
|--|--------------|--------------|------------------|------------------|------------------|------------|------------|------------------|------------------|------------|------------|------------|------------------|------------------|------------|-----|
| G۱   | y Glr        | n Ala        | a Gly            | Se 325           |                  | lle        | Ser        | Asn              | Ser<br>330       |            | Ala        | Gln        |                  | Phe 335          | Asp        |     |
| Ph   | e Pro        | Asp          | Asp<br>340       |                  | n Glm            | Asn        | Ser        | Lys<br>345       |                  | Leu        | ıAla       | Ala        | Gly<br>350       |                  | Glu        |     |
| Lei  | u Glr        | 9 Pro<br>355 |                  | Ala              | ı lle            | Val        | Asp<br>360 |                  | Arg              | Pro        | Ser        | Ser<br>365 | _                | Ala              | Ser        |     |
| Se   | r Arg<br>370 |              | Ser              | Ser              | Arg              | Pro<br>375 |            | Pro              | Asp              | Asp        | Leu<br>380 |            | lle              |                  |            |     |
| <210> 114<br><211> 3074<br><212> DNA<br><213> Homo sapiens   |              |              |                  |                  |                  |            |            |                  |                  |            |            |            |                  |                  |            |     |
| <220> <221> CDS <222> (201) (1346)   |              |              |                  |                  |                  |            |            |                  |                  |            |            |            |                  |                  |            |     |
| <400> 114 aactttacg aggtatcagc actttcttt cattaggggg aaggcgtgag gaaagtacca 60   |              |              |                  |                  |                  |            |            |                  |                  |            |            |            |                  | 60               |            |     |
| aacagcagcg gagttttaaa ctttaaatag acaggtctga gtgcctgaac ttgccttttc 12   |              |              |                  |                  |                  |            |            |                  |                  |            |            |            |                  | 120              |            |     |
| attttacttc atcctccaag gagttcaatc acttggcgtg acttcactac ttttaagcaa 1  |              |              |                  |                  |                  |            |            |                  |                  |            |            |            |                  | 180              |            |     |
| aagagtggtg cccaggcaac atg ggt gac tgg agc gcc tta ggc aaa ctc ctt 2<br>Met Gly Asp Trp Ser Ala Leu Gly Lys Leu Leu<br>1 5 10 |              |              |                  |                  |                  |            |            |                  |                  |            |            |            |                  | 233              |            |     |
| gac<br>Asp   | aag<br>Lys   | gtt<br>Val   | caa<br>Gln<br>15 | gcc<br>Ala       | tac<br>Tyr       | tca<br>Ser | act<br>Thr | gct<br>Ala<br>20 | gga<br>Gly       | ggg<br>Gly | aag<br>Lys | gtg<br>Val | tgg<br>Trp<br>25 | ctg<br>Leu       | tca<br>Ser | 281 |
|  |              |              |                  |                  | cga<br>Arg       |            |            |                  |                  |            |            |            |                  |                  |            | 329 |
|  |              |              |                  |                  | cag<br>Gln       |            |            |                  |                  |            |            |            |                  |                  |            | 377 |
|  |              |              |                  |                  | tgc<br>Cys<br>65 |            |            |                  |                  |            |            |            |                  |                  |            | 425 |
| cgc<br>Arg   | ttc<br>Phe   | tgg<br>Trp   | gtc<br>Val       | ctg<br>Leu<br>80 | cag<br>Gln       | atc<br>Ile | ata<br>He  | ttt<br>Phe       | gtg<br>Val<br>85 | tct<br>Ser | gta<br>Val | ccc<br>Pro | aca<br>Thr       | ctc<br>Leu<br>90 | ttg<br>Leu | 473 |
| tac<br>Tyr   | ctg<br>Leu   | gct<br>Ala   | cat<br>His       | gtg<br>Val       | ttc<br>Phe       | tat<br>Tyr | gtg<br>Val | atg<br>Met       | cga<br>Arg       | aag<br>Lys | gaa<br>Glu | gag<br>Glu | aaa<br>Lys       | ctg<br>Leu       | aac<br>Asn | 521 |

aag aaa gag gaa gaa ctc aag gtt gcc caa act gat ggt gtc aat gtg

| Lys | Lys | Glu<br>110 | Glu | GIU | Lys               | Val<br>115 | Ala | Gln | Thr | Asp | Gly<br>120 | V | Asn | Val |      |
|-----|-----|------------|-----|-----|-------------------|------------|-----|-----|-----|-----|------------|---|-----|-----|------|
|     |     |            |     |     | att<br>  e<br> 30 |            |     |     |     |     |            |   |     |     | 617  |
|     |     |            |     |     | aaa<br>Lys        |            |     |     |     |     |            |   |     |     | 665  |
|     |     |            |     |     | aag<br>Lys        |            |     |     |     |     |            |   |     |     | 713  |
|     |     |            |     |     | gga<br>Gly        |            |     |     |     |     |            |   |     |     | 761  |
|     |     |            |     |     | cat<br>His        |            |     |     |     |     |            |   |     |     | 809  |
|     |     |            |     |     | atc<br>lle<br>210 |            |     |     |     |     |            |   |     |     | 857  |
|     |     |            |     |     | att<br>lle        |            |     |     |     |     |            |   |     |     | 905  |
|     |     |            |     |     | gga<br>Gly        |            |     |     |     |     |            |   |     |     | 953  |
|     |     |            |     |     | aaa<br>Lys        |            |     |     |     |     |            |   |     |     | 1001 |
|     |     |            |     |     | cca<br>Pro        |            |     |     |     |     |            |   |     |     | 1049 |
|     |     |            |     |     | act<br>Thr<br>290 |            |     |     |     |     |            |   |     |     | 1097 |
|     |     |            |     |     | agt<br>Ser        |            |     |     |     |     |            |   |     |     | 1145 |
|     |     |            |     |     | cag<br>Gln        |            |     |     |     |     |            |   |     |     | 1193 |
|     |     |            |     |     | ccc<br>Pro        |            |     |     |     |     |            |   |     |     | 1241 |

|                                 |                                   | •                                |                            |                                 |                        |      |
|---------------------------------|-----------------------------------|----------------------------------|----------------------------|---------------------------------|------------------------|------|
| gct gct gg<br>Ala Ala Gl<br>35  | ga cat gaa d<br>y His Glu L<br>50 | ca cag cca<br>Leu Gln Pro<br>355 | cta gcc att<br>Leu Ala Ile | gtg gac ca<br>Val Asp GI<br>360 | g cga cct<br>n Arg Pro | 1289 |
|                                 | ga gcc agc a<br>g Ala Ser S       |                                  |                            |                                 |                        | 1337 |
| ctg gag at<br>Leu Glu II<br>380 | c tagatacag<br>e                  | gg cttgaaagc                     | a tcaagatto                | c actcaattg                     | t                      | 1386 |
| ggagaagaaa                      | aaaggtgctg                        | tagaaagtgo                       | accaggtgtt                 | aattttgatc                      | cggtggaggt             | 1446 |
| ggtactcaac                      | agccttattc                        | atgaggctta                       | gaaaacacaa                 | agacattaga                      | atacctaggt             | 1506 |
| tcactggggg                      | tgtatggggt                        | agatgggtgg                       | agagggaggg                 | gataagagag                      | gtgcatgttg             | 1566 |
| gtatttaaag                      | tagtggattc                        | aaagaactta                       | gattataaat                 | aagagttcca                      | ttaggtgata             | 1626 |
|                                 | ggctttttct                        |                                  |                            |                                 |                        |      |
|                                 | taattgtggc                        |                                  |                            |                                 |                        |      |
|                                 | atacttcctg                        |                                  |                            |                                 |                        |      |
|                                 | ccctgctaaa                        |                                  |                            |                                 |                        |      |
|                                 | ccctccaggt                        |                                  |                            |                                 |                        |      |
|                                 |                                   |                                  |                            |                                 |                        |      |
|                                 | attcagacaa                        |                                  |                            |                                 |                        |      |
|                                 | tccatccact                        |                                  |                            |                                 | _                      |      |
|                                 | cattcattta                        |                                  |                            |                                 |                        |      |
| ttaacatttt                      | ttttttgagc                        | taaagtcagg                       | gaatcaagcc                 | atgcttaata                      | tttaacaatc             | 2166 |
| acttatatgt                      | gtgtcgaaga                        | gtttgttttg                       | tttgtcatgt                 | attggtacaa                      | gcagatacag             | 2226 |
| tataaactca                      | caaacacaga                        | tttgaaaata                       | atgcacatat                 | ggtgttcaaa                      | tttgaacctt             | 2286 |
| tctcatggat                      | ttttgtggtg                        | tgggccaata                       | tggtgtttac                 | attatataat                      | tcctgctgtg             | 2346 |
| gcaagtaaag                      | cacactttt                         | ttttctccta                       | aaatgtttt                  | ccctgtgtat                      | cctattatgg             | 2406 |
| atactggttt                      | tgttaattat                        | gattctttat                       | tttctctcct                 | ttttttagga                      | tatagcagta             | 2466 |
| atgctattac                      | tgaaatgaat                        | ttcctttttc                       | tgaaatgtaa                 | tcattgatgc                      | ttgaatgata             | 2526 |
| gaattttagt                      | actgtaaaca                        | ggctttagtc                       | attaatgtga                 | gagacttaga                      | aaaaaatgct             | 2586 |
| tagagtggac                      | tattaaatgt                        | gcctaaatga                       | attttgcagt                 | aactggtatt                      | cttgggtttt             | 2646 |
| cctacttaat                      | acacagtaat                        | tcagaacttg                       | tattctatta                 | tgagtttagc                      | agtcttttgg             | 2706 |
|                                 |                                   |                                  |                            |                                 |                        | 0700 |

 ${\tt agtgaccagc} \ \ {\tt aactttgatg} \ \ {\tt tttgcactaa} \ \ {\tt gattttattt} \ \ {\tt ggaatgcaag} \ \ {\tt agaggttgaa} \ \ 2766$ 

agaggattca gtagtacaca tacaactaat ttatttgaac tatatgttga agacatctac 2826 cagtttctcc aaatgccttt tttaaaactc atcacagaag attggtgaaa atgctgagta 2886 tgacactttt cttcttgcat gcatgtcagc tacataaaca gttttgtaca atgaaaatta 2946 ctaatttgtt tgacattcca tgttaaacta cggtcatgtt cagcttcatt gcatgtaatg 3006 tagacctagt ccatcagatc atgtgttctg gagagtgttc tttattcaat aaagttttaa 3066 tttagtat

<210> 115

<211> 382

<212> PRT

<213> Homo sapiens

<400> 115

Met Gly Asp Trp Ser Ala Leu Gly Lys Leu Leu Asp Lys Val Gln Ala 1 5 10 15

Tyr Ser Thr Ala Gly Gly Lys Val Trp Leu Ser Val Leu Phe 11e Phe 20 25 30

Arg IIe Leu Leu Gly Thr Ala Val Glu Ser Ala Trp Gly Asp Glu 35 40 45

Gln Ser Ala Phe Arg Cys Asn Thr Gln Gln Pro Gly Cys Glu Asn Val 50 55 60

Cys Tyr Asp Lys Ser Phe Pro IIe Ser His Val Arg Phe Trp Val Leu 65 70 75 80

Gln lle lle Phe Val Ser Val Pro Thr Leu Leu Tyr Leu Ala His Val 85 90 95

Phe Tyr Val Met Arg Lys Glu Glu Lys Leu Asn Lys Lys Glu Glu Glu 100 105 110

Leu Lys Val Ala Gln Thr Asp Gly Val Asn Val Asp Met His Leu Lys 115 120 125

Gln lle Glu lle Lys Lys Phe Lys Tyr Gly lle Glu Glu His Gly Lys 130 135 140

Val Lys Met Arg Gly Gly Leu Leu Arg Thr Tyr lle lle Ser lle Leu 145 150 155 160

Phe Lys Ser IIe Phe Glu Val Ala Phe Leu Leu IIe Gln Trp Tyr IIe 165 170 175

Tyr Gly Phe Ser Leu Ser Ala Val Tyr Thr Cys Lys Arg Asp Pro Cys 180 185 190

Pro His Gln Val Asp Cys Phe Leu Ser Arg Pro Thr Glu Lys Thr 11e 195 200 205

Phe lle lle Phe Met Leu Val Val Ser Leu Val Ser Leu Ala Leu Asn lle lle Glu Leu Phe Tyr Val Phe Phe Lys Gly Val Lys Asp Arg Val Lys Gly Lys Ser Asp Pro Tyr His Ala Thr Ser Gly Ala Leu Ser Pro Ala Lys Asp Cys Gly Ser Gln Lys Tyr Ala Tyr Phe Asn Gly Cys Ser Ser Pro Thr Ala Pro Leu Ser Pro Met Ser Pro Pro Gly Tyr Lys Leu Val Thr Gly Asp Arg Asn Asn Ser Ser Cys Arg Asn Tyr Asn Lys Gln Ala Ser Glu Gln Asn Trp Ala Asn Tyr Ser Ala Glu Gin Asn Arg Met 315 Gly Gln Ala Gly Ser Thr Ile Ser Asn Ser His Ala Gln Pro Phe Asp 335 Phe Pro Asp Asp Asn Gln Asn Ser Lys Leu Ala Ala Gly His Glu Leu Gln Pro Leu Ala Ile Val Asp Gln Arg Pro Ser Ser Arg Ala Ser Ser Arg Ala Ser Ser Arg Pro Arg Pro Asp Asp Leu Glu Ile <210> 116 <211> 3074 <212> DNA

<210> 116 <211> 3074 <212> DNA <213> Homo sapiens <220> <221> CDS <222> (201).. (1346)

<400> 116
aacttttacg aggtatcagc acttttcttt cattaggggg aaggcgtgag gaaagtacca 60
aacagcagcg gagtttaaa ctttaaatag acaggtctga gtgcctgaac ttgcctttc 120
atttacttc atcctccaag gagttcaatc acttggcgtg acttcactac ttttaagcaa 180
aagagtggtg cccaggcaac atg ggt gac tgg agc gcc tta ggc aaa ctc ctt 233
Met Gly Asp Trp Ser Ala Leu Gly Lys Leu Leu
1
5
10

gac aag gtt caa gcc tac tca act gct gga ggg aag gtg tgg ctg tca 281 Asp Lys Val Gln Ala Tyr Ser Thr Ala Gly Gly Lys Val Trp Leu Ser 15 20 25

|           |                   |                  |            | •                 |            |            |                  |            |                   |            |            |                  | <b>\</b>   |                   |            |      |
|-----------|-------------------|------------------|------------|-------------------|------------|------------|------------------|------------|-------------------|------------|------------|------------------|------------|-------------------|------------|------|
| gt:<br>Va | a ctt<br>I Leu    | ttc<br>Phe<br>30 | att<br>He  | ttc<br>Phe        | cga<br>Arg | atc<br>He  | ctg<br>Leu<br>35 | ctg<br>Leu | ctg<br>Leu        | ggg<br>Gly | aca<br>Thr | gcg<br>Ala<br>40 | gtt<br>Val | gag<br>Glu        | tca<br>Ser | 329  |
|           | tgg<br>Trp<br>45  | Gly              |            |                   |            |            |                  |            |                   |            |            |                  |            |                   |            | 377  |
|           | tgt<br>Cys<br>(   |                  |            |                   |            |            |                  |            |                   |            |            |                  |            |                   |            | 425  |
|           | ttc<br>Phe        |                  |            |                   |            |            |                  |            |                   |            |            |                  |            |                   |            | 473  |
|           | ctg<br>Leu        |                  |            |                   |            |            |                  |            |                   |            |            |                  |            |                   |            | 521  |
|           | g aaa<br>s Lys    |                  |            |                   |            |            |                  |            |                   |            |            |                  |            |                   |            | 569  |
|           | atg<br>Met<br>125 |                  |            |                   |            |            |                  |            |                   |            |            |                  |            |                   |            | 617  |
|           | gag<br>Glu        |                  |            |                   |            |            |                  |            |                   |            |            |                  |            |                   |            | 665  |
| ato<br>He | atc               | agt<br>Ser       | atc<br>Ile | ctc<br>Leu<br>160 | ttc<br>Phe | aag<br>Lys | tct<br>Ser       | atc<br>Ile | ttt<br>Phe<br>165 | gag<br>Glu | gtg<br>Val | gcc<br>Ala       | ttc<br>Phe | ttg<br>Leu<br>170 | ctg<br>Leu | 713  |
|           | cag<br>Gln        |                  |            |                   |            |            |                  |            |                   |            |            |                  |            |                   |            | 761  |
|           | aga<br>Arg        |                  |            |                   |            |            |                  |            |                   |            |            |                  |            |                   |            | 809  |
|           | gag<br>Glu<br>205 |                  |            |                   |            |            |                  |            |                   |            |            |                  |            |                   |            | 857  |
|           | ctg<br>Leu        |                  |            |                   |            |            |                  |            |                   |            |            |                  |            |                   |            | 905  |
|           | aag<br>Lys        |                  |            |                   |            |            |                  |            |                   |            |            |                  |            |                   |            | 953  |
| ggt       | gcg               | ctg              | agc        | cct               | gcc        | aaa        | gac              | tgt        | ggg               | tct        | саа        | aaa              | tat        | gct               | tat        | 1001 |

| Gly Ala Leu Ser Produce Lys Asp Cys Gly Ser Gln Lys 1 Ala Tyr 255 260  |     |
|--|-----|
| ttc aat ggc tgc tcc tca cca acc gct ccc ctc tcg cct atg tct cct Phe Asn Gly Cys Ser Ser Pro Thr Ala Pro Leu Ser Pro Met Ser Pro 270 275 280          | 49  |
| cct ggg tac aag ctg gtt act ggc gac aga aac aat tct tct tgc cgc 10<br>Pro Gly Tyr Lys Leu Val Thr Gly Asp Arg Asn Asn Ser Ser Cys Arg<br>285 290 295 | 97  |
| aat tac aac aag caa gca agt gag caa aac tgg gct aat tac agt gca Asn Tyr Asn Lys Gln Ala Ser Glu Gln Asn Trp Ala Asn Tyr Ser Ala 300 305 310 315      | 45  |
| gaa caa aat cga atg ggg cag gcg gga agc acc atc tct aac tcc cat Glu Gln Asn Arg Met Gly Gln Ala Gly Ser Thr Ile Ser Asn Ser His 320 325 330          | 93  |
| gca cag cct ttt gat ttc ccc gat gat aac cag aat tct aaa aaa cta 12<br>Ala Gln Pro Phe Asp Phe Pro Asp Asp Asn Gln Asn Ser Lys Lys Leu<br>335 340 345 | 241 |
| gct gct gga cat gaa tta cag cca cta gcc att gtg gac cag cga cct 12<br>Ala Ala Gly His Glu Leu Gln Pro Leu Ala Ile Val Asp Gln Arg Pro<br>350 355 360 | 289 |
| tca agc aga gcc agc agt cgt gcc agc agc aga cct cgg cct gat gac Ser Ser Arg Ala Ser Ser Arg Ala Ser Ser Arg Pro Arg Pro Asp Asp 365 370 375          |     |
| ctg gag atc tagatacagg cttgaaagca tcaagattcc actcaattgt 13<br>Leu Glu Ile<br>380   | 886 |
| ggagaagaaa aaaggtgctg tagaaagtgc accaggtgtt aattttgatc cggtggaggt 14   | 46  |
| ggtactcaac agccttattc atgaggctta gaaaacacaa agacattaga atacctaggt 15   | 06  |
| tcactggggg tgtatggggt agatgggtgg agagggaggg gataagagag gtgcatgttg 15   | 66  |
| gtatttaaag tagtggattc aaagaactta gattataaat aagagttcca ttaggtgata 16   | 526 |
| catagataag ggcttttct ccccgcaaac acccctaaga atggttctgt gtatgtgaat 16  | 386 |
| gagcgggtgg taattgtggc taaatatttt tgttttacca agaaactgaa ataattctgg 17   | 146 |
| ccaggaataa atacttcctg aacatcttag gtcttttcaa caagaaaaag acagaggatt 18   |     |
| gtccttaagt ccctgctaaa acattccatt gttaaaattt gcactttgaa ggtaagcttt 18   |     |
| ctaggcctga ccctccaggt gtcaatggac ttgtgctact atatttttt attcttggta 19  |     |
| tcagtttaaa attcagacaa ggcccacaga ataagatttt ccatgcattt gcaaatacgt 19   |     |
| atattettt teeateeact tgeacaatat cattaceate acttttteat catteeteag 20  |     |
| ctactactca cattcattta atggtttctg taaacatttt taagacagtt gggatgtcac 21   | טטו |

ttaacatttt ttttttgagc taaagtcagg gaatcaagcc atgcttaata tttaacaatc 2166 acttatatgt gtgtcgaaga gtttgttttg tttgtcatgt attggtacaa gcagatacag 2226 tataaactca caaacacaga tttgaaaata atgcacatat ggtgttcaaa tttgaacctt 2286 tctcatggat ttttgtggtg tgggccaata tggtgtttac attatataat tcctgctgtg 2346 gcaagtaaag cacacttttt ttttctccta aaatgttttt ccctgtgtat cctattatgg 2406 atactggttt tgttaattat gattctttat tttctctcct ttttttagga tatagcagta 2466 atgctattac tgaaatgaat ttccttttc tgaaatgtaa tcattgatgc ttgaatgata 2526 gaattttagt actgtaaaca ggctttagtc attaatgtga gagacttaga aaaaaatgct 2586 tagagtggac tattaaatgt gcctaaatga attttgcagt aactggtatt cttgggtttt 2646 cctacttaat acacagtaat tcagaacttg tattctatta tgagtttagc agtcttttgg 2706 agtgaccagc aactttgatg tttgcactaa gattttattt ggaatgcaag agaggttgaa 2766 agaggattca gtagtacaca tacaactaat ttatttgaac tatatgttga agacatctac 2826 cagtttctcc aaatgccttt tttaaaactc atcacagaag attggtgaaa atgctgagta 2886 tgacactttt cttcttgcat gcatgtcagc tacataaaca gttttgtaca atgaaaatta 2946 ctaatttgtt tgacattcca tgttaaacta cggtcatgtt cagcttcatt gcatgtaatg 3006 tagacctagt ccatcagatc atgtgttctg gagagtgttc tttattcaat aaagttttaa 3066 3074 tttagtat

<400> 117

Met Glu Gly Ala Ala Leu Leu Arg Val Ser Val Leu Cys Ile Trp Met 1 5 10 15

Ser Ala Leu Phe Leu Gly Val Gly Val Arg Ala Glu Glu Ala Gly Ala 20 25 30

Arg Val Gln Gln Asn Val Pro Ser Gly Thr Asp Thr Gly Asp Pro Gln 35 40 45

Ser Lys Pro Leu Gly Asp Trp Ala Ala Gly Thr Met Asp Pro Glu Ser 50 55 60

Ser lle Phe lle Glu Asp Ala lle Lys Tyr Phe Lys Glu Lys Val Ser 65 70 75 80

Thr Gln Asn Leu Leu Leu Leu Thr Asp Asn Glu Ala Trp Asn Gly

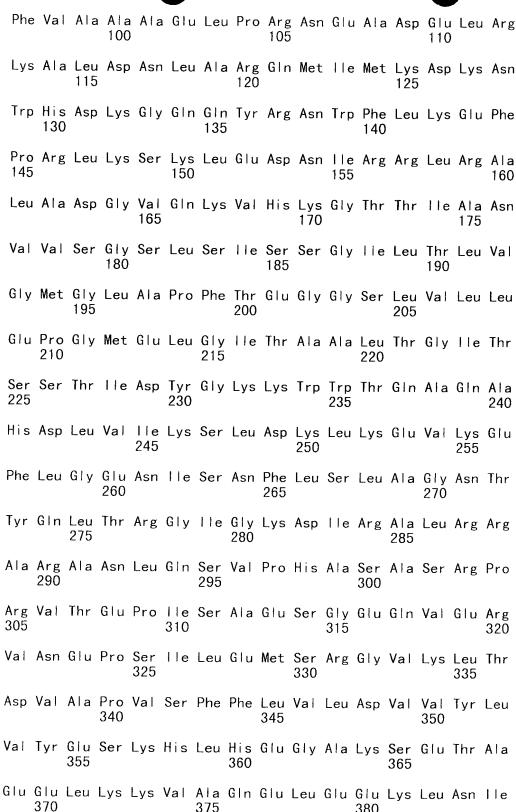
<sup>&</sup>lt;210> 117

<sup>&</sup>lt;211> 398

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens





Leu Asn Asn Asn Tyr Lys lie Leu Gln Ala Asp Gln Glu Leu

| <21<br><21        | 0> 1<br>1> 2<br>2> E<br>3> F | 2054<br>NA       | sapi              | ens               |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |     |
|-------------------|------------------------------|------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-----|
|                   | 20><br>21> C<br>22> (        |                  | . (12             | 269)              |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |     |
|                   | 0> 1<br>acag                 |                  | agaa              | cago              | tg g              | atct              | tgct              | c ag              | tctc              | tgcc              | : agg             | ggaa              | gat               | tcct              | tggagg            | 60  |
| agg               | ccct                         | gca              | gcga              |                   |                   |                   |                   | a Al              |                   |                   |                   |                   | I Se              |                   | c ctc<br>I Leu    | 111 |
| tgc<br>Cys        | atc<br>He                    | tgg<br>Trp<br>15 | Met               | agt<br>Ser        | gca<br>Ala        | ctt<br>Leu        | ttc<br>Phe<br>20  | ctt<br>Leu        | ggt<br>Gly        | gtg<br>Val        | gga<br>Gly        | gtg<br>Val<br>25  | agg<br>Arg        | gca<br>Ala        | gag<br>Glu        | 159 |
| gaa<br>Glu        | gct<br>Ala<br>30             | gga<br>Gly       | gcg<br>Ala        | agg<br>Arg        | gtg<br>Val        | caa<br>Gln<br>35  | caa<br>Gin        | aac<br>Asn        | gtt<br>Vai        | cca<br>Pro        | agt<br>Ser<br>40  | ggg<br>Gly        | aca<br>Thr        | gat<br>Asp        | act<br>Thr        | 207 |
| gga<br>Gly<br>45  | gat<br>Asp                   | cct<br>Pro       | caa<br>Gln        | agt<br>Ser        | aag<br>Lys<br>50  | ccc<br>Pro        | ctc<br>Leu        | ggt<br>Gly        | gac<br>Asp        | tgg<br>Trp<br>55  | gct<br>Ala        | gct<br>Ala        | ggc<br>Gly        | acc<br>Thr        | atg<br>Met<br>60  | 255 |
| gac<br>Asp        | cca<br>Pro                   | gag<br>Glu       | agc<br>Ser        | agt<br>Ser<br>65  | atc<br>lle        | ttt<br>Phe        | att<br>He         | gag<br>Glu        | gat<br>Asp<br>70  | gcc<br>Ala        | att<br>He         | aag<br>Lys        | tat<br>Tyr        | ttc<br>Phe<br>75  | aag<br>Lys        | 303 |
| gaa<br>Glu        | aaa<br>Lys                   | gtg<br>Val       | agc<br>Ser<br>80  | aca<br>Thr        | cag<br>Gln        | aat<br>Asn        | ctg<br>Leu        | cta<br>Leu<br>85  | ctc<br>Leu        | ctg<br>Leu        | ctg<br>Leu        | act<br>Thr        | gat<br>Asp<br>90  | aat<br>Asn        | gag<br>Glu        | 351 |
| gcc<br>Ala        | tgg<br>Trp                   | aac<br>Asn<br>95 | gga<br>Gly        | ttc<br>Phe        | gtg<br>Val        | gct<br>Ala        | gct<br>Ala<br>100 | gct<br>Ala        | gaa<br>Glu        | ctg<br>Leu        | ccc<br>Pro        | agg<br>Arg<br>105 | aat<br>Asn        | gag<br>Glu        | gca<br>Ala        | 399 |
| gat<br>Asp        | gag<br>Glu<br>110            | ctc<br>Leu       | cgt<br>Arg        | aaa<br>Lys        | gct<br>Ala        | ctg<br>Leu<br>115 | gac<br>Asp        | aac<br>Asn        | ctt<br>Leu        | gca<br>Ala        | aga<br>Arg<br>120 | caa<br>Gln        | atg<br>Met        | atc<br>lle        | atg<br>Met        | 447 |
| aaa<br>Lys<br>125 | gac<br>Asp                   | aaa<br>Lys       | aac<br>Asn        | tgg<br>Trp        | cac<br>His<br>130 | gat<br>Asp        | aaa<br>Lys        | ggc<br>Gly        | cag<br>Gln        | cag<br>Gln<br>135 | tac<br>Tyr        | aga<br>Arg        | aac<br>Asn        | tgg<br>Trp        | ttt<br>Phe<br>140 | 495 |
| ctg<br>Leu        | aaa<br>Lys                   | gag<br>Glu       | ttt<br>Phe        | cct<br>Pro<br>145 | cgg<br>Arg        | ttg<br>Leu        | aaa<br>Lys        | agt<br>Ser        | aag<br>Lys<br>150 | ctt<br>Leu        | gag<br>Glu        | gat<br>Asp        | aac<br>Asn        | ata<br>Ile<br>155 | aga<br>Arg        | 543 |
| agg<br>Arg        | ctc<br>Leu                   | cgt<br>Arg       | gcc<br>Ala<br>160 | ctt<br>Leu        | gca<br>Ala        | gat<br>Asp        | ggg<br>Gly        | gtt<br>Val<br>165 | cag<br>Gln        | aag<br>Lys        | gtc<br>Val        | cac<br>His        | aaa<br>Lys<br>170 | ggc<br>Gly        | acc<br>Thr        | 591 |

| ac<br>Th          | c at<br>r          | c gc<br>e Al<br>17  | a AS                  | t gt:<br>n Va     | g<br>  Va         | g to                  | t ggd<br>r Gly<br>180 | / Se              | t cte             | c ag<br>u Se         | c ati<br>r lle        | t tcc<br>e Ser<br>185 | Sei               | gg<br>Gly         | c atc<br>y lle      | 639  |
|-------------------|--------------------|---------------------|-----------------------|-------------------|-------------------|-----------------------|-----------------------|-------------------|-------------------|----------------------|-----------------------|-----------------------|-------------------|-------------------|---------------------|------|
| ct<br>Le          | g ac<br>u Th<br>19 | r Le                | c gto<br>u Va         | c ggo<br>I Gly    | c atg<br>/ Me     | g ggt<br>t Gly<br>195 | / Lei                 | g gca<br>ı Ala    | a cce<br>a Pre    | c tte<br>o Phe       | c aca<br>e Thr<br>200 | Glu                   | g gga<br>i Gly    | aggo<br>Gly       | c agc<br>/ Ser      | 687  |
| ct<br>Le<br>20    | u va               | a cte               | c ttg<br>u Lei        | g gaa<br>u Glu    | 210               | o Giy                 | g atg<br>⁄Met         | gag<br>Glu        | g ttg<br>ı Lei    | g gga<br>u Gly<br>21 | y lle                 | aca<br>Thr            | gca<br>Ala        | a got<br>a Ala    | t ttg<br>Leu<br>220 | 735  |
| acc<br>Th         | c ggg<br>r Gly     | g ati<br>y lle      | t acc<br>e Thr        | ago<br>Ser<br>225 | Ser               | acc<br>Thr            | ata<br> -             | gac<br>Asp        | tac<br>Tyr<br>230 | ′ Gly                | a aag<br>/ Lys        | aag<br>Lys            | tgg<br>Trp        | tgg<br>Trp<br>235 |                     | 783  |
| caa<br>Glr        | a gco<br>n Ala     | c caa<br>a Gir      | a gcc<br>n Ala<br>240 | HIS               | gac<br>Asp        | ctg<br>Leu            | gtc<br>Val            | ato<br>He<br>245  | Lys               | a ago<br>Ser         | ctt<br>Leu            | gac<br>Asp            | aaa<br>Lys<br>250 | Leu               | aag<br>Lys          | 831  |
| gag<br>Glu        | g gtg<br>ı Val     | g aag<br>Lys<br>255 | Glu                   | ttt<br>Phe        | ttg<br>Leu        | ggt<br>Gly            | gag<br>Glu<br>260     | aac<br>Asn        | ata<br>Ile        | tcc<br>Ser           | aac<br>Asn            | ttt<br>Phe<br>265     | ctt<br>Leu        | tcc<br>Ser        | tta<br>Leu          | 879  |
| gct<br>Ala        | ggc<br>Gly<br>270  | Asn                 | act<br>Thr            | tac<br>Tyr        | caa<br>G n        | ctc<br>Leu<br>275     | aca<br>Thr            | cga<br>Arg        | ggc<br>Gly        | att<br>Ile           | ggg<br>Gly<br>280     | aag<br>Lys            | gac<br>Asp        | atc<br>ile        | cgt<br>Arg          | 927  |
| gcc<br>Ala<br>285 | Leu                | aga<br>Arg          | cga<br>Arg            | gcc<br>Ala        | aga<br>Arg<br>290 | gcc<br>Ala            | aat<br>Asn            | ctt<br>Leu        | cag<br>Gln        | tca<br>Ser<br>295    | gta<br>Val            | ccg<br>Pro            | cat<br>His        | gcc<br>Ala        | tca<br>Ser<br>300   | 975  |
| gcc<br>Ala        | tca<br>Ser         | cgc<br>Arg          | ccc<br>Pro            | cgg<br>Arg<br>305 | gtc<br>Val        | act<br>Thr            | gag<br>Glu            | cca<br>Pro        | atc<br>lle<br>310 | tca<br>Ser           | gct<br>Ala            | gaa<br>Glu            | agc<br>Ser        | ggt<br>Gly<br>315 | gaa<br>Glu          | 1023 |
| cag<br>Gln        | gtg<br>Val         | gag<br>Glu          | aga<br>Arg<br>320     | ٧a١               | Asn               | gaa<br>Glu            | Pro                   | agc<br>Ser<br>325 | Пe                | ctg<br>Leu           | gaa<br>Glu            | Met                   | agc<br>Ser<br>330 | aga<br>Arg        | gga<br>Gly          | 1071 |
| gtc<br>Val        | aag<br>Lys         | ctc<br>Leu<br>335   | acg<br>Thr            | gat<br>Asp        | gtg<br>Val        | Ala                   | cct<br>Pro<br>340     | gta<br>Val        | agc<br>Ser        | ttc<br>Phe           | ttt<br>Phe            | ctt<br>Leu<br>345     | gtg<br>Val        | ctg<br>Leu        | gat<br>Asp          | 1119 |
| gta<br>Val        | gtc<br>Val<br>350  | tac<br>Tyr          | ctc<br>Leu            | gtg<br>Val        | tac<br>Tyr        | gaa<br>Glu<br>355     | tca<br>Ser            | aag<br>Lys        | cac<br>His        | tta<br>Leu           | cat<br>His<br>360     | gag<br>Glu            | ggg<br>Gly        | gca<br>Ala        | aag<br>Lys          | 1167 |
| tca<br>Ser<br>365 | gag<br>Glu         | aca<br>Thr          | gct<br>Ala            | Glu               | gag<br>Glu<br>370 | ctg<br>Leu            | aag l<br>Lys l        | aag<br>Lys        | Val               | gct<br>Ala<br>375    | cag<br>Gln            | gag (<br>Glu l        | ctg<br>Leu        | Glu               | gag<br>Glu<br>380   | 1215 |
| aag<br>Lys        | cta<br>Leu         | aac<br>Asn          | He                    | ctc<br>Leu<br>385 | aac<br>Asn        | aat .<br>Asn .        | aat t<br>Asn T        | Tyr I             | aag<br>Lys<br>390 | att<br>He            | ctg (<br>Leu (        | cag g<br>Gln <i>A</i> | Ala /             | gac<br>Asp<br>395 | caa<br>Gin          | 1263 |
| gaa<br>Glu        | ctg<br>Leu         | tgac                | caca                  | gg go             | cagg              | gcago                 | c cad                 | ccag              | gaga              | gat                  | atgco                 | ctg g                 | gcag              | gggc              | са                  | 1319 |

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gctcagatct ctagagctgt cttgtcccc cccaggattg acctgtgtaa gtcccaataa 2039
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<400> 119

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10 15

Ser Ala Leu Phe Leu Gly Val Arg Val Arg Ala Glu Glu Ala Gly Ala 20 25 30

Arg Val Gln Gln Asn Val Pro Ser Gly Thr Asp Thr Gly Asp Pro Gln
35 40 45

Ser Lys Pro Leu Gly Asp Trp Ala Ala Gly Thr Met Asp Pro Glu Ser 50 60

Ser lle Phe lle Glu Asp Ala lle Lys Tyr Phe Lys Glu Lys Val Ser 65 70 75 80

Thr Gin Asn Leu Leu Leu Leu Leu Thr Asp Asn Giu Ala Trp Asn Giy 85 90 95

Phe Val Ala Ala Glu Leu Pro Arg Asn Glu Ala Asp Glu Leu Arg 100 105 110

Lys Ala Leu Asp Asn Leu Ala Arg Gln Met lle Met Lys Asp Lys Asn 115 120 125

<sup>&</sup>lt;210> 119

<sup>&</sup>lt;211> 398

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

Trp His Asp Lys Gly n Gln Tyr Arg Asn Trp Phe Leu Leu Glu Phe Pro Arg Leu Lys Ser Lys Leu Glu Asp Asn Ile Arg Arg Leu Arg Ala Leu Ala Asp Gly Val Gln Lys Val His Lys Gly Thr Thr lie Ala Asn Val Val Ser Gly Ser Leu Ser Ile Ser Ser Gly Ile Leu Thr Leu Val Gly Met Gly Leu Ala Pro Phe Thr Glu Gly Gly Ser Leu Val Leu Leu 200 Glu Pro Gly Met Glu Leu Gly lle Thr Ala Ala Leu Thr Gly lle Thr Ser Ser Thr lle Asp Tyr Gly Lys Lys Trp Trp Thr Gln Ala Gln Ala 225 235 240 His Asp Leu Val IIe Lys Ser Leu Asp Lys Leu Lys Glu Val Lys Glu Phe Leu Gly Glu Asn Ile Ser Asn Phe Leu Ser Leu Ala Gly Asn Thr 265 Tyr Gln Leu Thr Arg Gly lle Gly Lys Asp lle Arg Ala Leu Arg Arg Ala Arg Ala Asn Leu Gln Ser Val Pro His Ala Ser Ala Ser Arg Pro 295 Arg Val Thr Glu Pro lie Ser Ala Glu Ser Gly Glu Gln Val Glu Arg 315 Val Asn Glu Pro Ser lle Leu Glu Met Ser Arg Gly Val Lys Leu Thr 325 Asp Val Ala Pro Val Ser Phe Phe Leu Val Leu Asp Val Val Tyr Leu 345 Val Tyr Glu Ser Lys His Leu His Glu Gly Ala Lys Ser Glu Thr Ala 360 365 Glu Glu Leu Lys Lys Val Ala Gln Glu Leu Glu Glu Lys Leu Asn Ile Leu Asn Asn Asn Tyr Lys Ile Leu Gln Ala Asp Gln Glu Leu 390 395

<210> 120

<211> 2054

<212> DNA

<213> Homo sapiens

<220>



cacacagete agaacagetg gatettgete agtetetgee aggggaagat teettggagg 60

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  Met Glu Gly Ala Ala Leu Leu Arg Val Ser Val Leu

  1 5 10
- tgc atc tgg atg agt gca ctt ttc ctt ggt gtg aga gtg agg gca gag
  Cys ile Trp Met Ser Ala Leu Phe Leu Gly Val Arg Val Arg Ala Glu
  15 20 25
- gaa gct gga gcg agg gtg caa caa aac gtt cca agt ggg aca gat act 207 Glu Ala Gly Ala Arg Val Gln Gln Asn Val Pro Ser Gly Thr Asp Thr 30 35 40
- gga gat cct caa agt aag ccc ctc ggt gac tgg gct gct ggc acc atg
  Gly Asp Pro Gln Ser Lys Pro Leu Gly Asp Trp Ala Ala Gly Thr Met
  45 50 55 60
- gac cca gag agc agt atc ttt att gag gat gcc att aag tat ttc aag
  Asp Pro Glu Ser Ser lle Phe lle Glu Asp Ala lle Lys Tyr Phe Lys
  65 70 75
- gaa aaa gtg agc aca cag aat ctg cta ctc ctg ctg act gat aat gag 351 Glu Lys Val Ser Thr Gln Asn Leu Leu Leu Leu Leu Thr Asp Asn Glu 80 85 90
- gcc tgg aac gga ttc gtg gct gct gct gaa ctg ccc agg aat gag gca 399 Ala Trp Asn Gly Phe Val Ala Ala Ala Glu Leu Pro Arg Asn Glu Ala 95 100 105
- gat gag ctc cgt aaa gct ctg gac aac ctt gca aga caa atg atc atg
  Asp Glu Leu Arg Lys Ala Leu Asp Asn Leu Ala Arg Gln Met Ile Met
  110 120
- aaa gac aaa aac tgg cac gat aaa ggc cag cag tac aga aac tgg ttt 495 Lys Asp Lys Asn Trp His Asp Lys Gly Gln Gln Tyr Arg Asn Trp Phe 125 130 140
- ctg aaa gag ttt cct cgg ttg aaa agt aag ctt gag gat aac ata aga 543 Leu Lys Glu Phe Pro Arg Leu Lys Ser Lys Leu Glu Asp Asn lie Arg
- agg ctc cgt gcc ctt gca gat ggg gtt cag aag gtc cac aaa ggc acc
  Arg Leu Arg Ala Leu Ala Asp Gly Val Gln Lys Val His Lys Gly Thr
  160 165 170
- acc atc gcc aat gtg gtg tct ggc tct ctc agc att tcc tct ggc atc
  Thr lie Ala Asn Val Val Ser Gly Ser Leu Ser lie Ser Ser Gly lie
  175
  180
  185
- ctg acc ctc gtc ggc atg ggt ctg gca ccc ttc aca gag gga ggc agc
  Leu Thr Leu Val Gly Met Gly Leu Ala Pro Phe Thr Glu Gly Gly Ser
  190 195 200

| ctt<br>Leu<br>205   | gta<br>Val        | ctc<br>Leu        | ttg<br>Leu        | ga:<br>Glu        | t<br>Pro<br>210   | ggg<br>Gly        | atg<br>Met        | gag<br>Glu        | ttg<br>Leu        | gga<br>Gly<br>215 | atc<br>lle        | aca<br>Thr        | a<br>Ala          | gct<br>Ala        | _                 | 735  |
|---------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| acc<br>Thr          | ggg<br>Gly        | att<br>  e        | acc<br>Thr        | agc<br>Ser<br>225 | agt<br>Ser        | acc<br>Thr        | ata<br>Ile        | gac<br>Asp        | tac<br>Tyr<br>230 | gga<br>Gly        | aag<br>Lys        | aag<br>Lys        | tgg<br>Trp        | tgg<br>Trp<br>235 | aca<br>Thr        | 783  |
| caa<br>G n          | gcc<br>Ala        | caa<br>Gln        | gcc<br>Ala<br>240 | cac<br>His        | gac<br>Asp        | ctg<br>Leu        | gtc<br>Val        | atc<br>  e<br>245 | aaa<br>Lys        | agc<br>Ser        | ctt<br>Leu        | gac<br>Asp        | aaa<br>Lys<br>250 | ttg<br>Leu        | aag<br>Lys        | 831  |
| gag<br>Glu          | gtg<br>Val        | aag<br>Lys<br>255 | gag<br>Glu        | ttt<br>Phe        | ttg<br>Leu        | ggt<br>Gly        | gag<br>Glu<br>260 | aac<br>Asn        | ata<br>He         | tcc<br>Ser        | aac<br>Asn        | ttt<br>Phe<br>265 | ctt<br>Leu        | tcc<br>Ser        |                   | 879  |
| gct<br>Ala          | ggc<br>Gly<br>270 | aat<br>Asn        | act<br>Thr        | tac<br>Tyr        | caa<br>Gln        | ctc<br>Leu<br>275 | aca<br>Thr        | cga<br>Arg        | ggc<br>Gly        | att<br>He         | ggg<br>Gly<br>280 | aag<br>Lys        | gac<br>Asp        | atc<br>Ile        | cgt<br>Arg        | 927  |
| gcc<br>A I a<br>285 | ctc<br>Leu        | aga<br>Arg        | cga<br>Arg        | gcc<br>Ala        | aga<br>Arg<br>290 | gcc<br>Ala        | aat<br>Asn        | ctt<br>Leu        | cag<br>Gln        | tca<br>Ser<br>295 | gta<br>Val        | ccg<br>Pro        | cat<br>His        | gcc<br>Ala        | tca<br>Ser<br>300 | 975  |
| gcc<br>Ala          | tca<br>Ser        | cgc<br>Arg        | ccc<br>Pro        | cgg<br>Arg<br>305 | gtc<br>Val        | act<br>Thr        | gag<br>Glu        | cca<br>Pro        | atc<br>lle<br>310 | tca<br>Ser        | gct<br>Ala        | gaa<br>Glu        | agc<br>Ser        | ggt<br>Gly<br>315 | gaa<br>Glu        | 1023 |
| cag<br>Gln          | gtg<br>Val        | gag<br>Glu        | aga<br>Arg<br>320 | gtt<br>Val        | aat<br>Asn        | gaa<br>Glu        | ccc<br>Pro        | agc<br>Ser<br>325 | atc<br>He         | ctg<br>Leu        | gaa<br>Glu        | atg<br>Met        | agc<br>Ser<br>330 | aga<br>Arg        | gga<br>Gly        | 1071 |
| gto<br>Val          | aag<br>Lys        | ctc<br>Leu<br>335 | acg<br>Thr        | gat<br>Asp        | gtg<br>Val        | gcc<br>Ala        | cct<br>Pro<br>340 | gta<br>Val        | agc<br>Ser        | ttc<br>Phe        | ttt<br>Phe        | ctt<br>Leu<br>345 | gtg<br>Val        | ctg<br>Leu        | gat<br>Asp        | 1119 |
| gta<br>Val          | gtc<br>Val<br>350 | tac<br>Tyr        | ctc<br>Leu        | gtg<br>Val        | tac<br>Tyr        | gaa<br>Glu<br>355 | tca<br>Ser        | aag<br>Lys        | His               | Leu               | cat<br>His<br>360 | gag<br>Glu        | ggg<br>Gly        | gca<br>Ala        | aag<br>Lys        | 1167 |
| tca<br>Ser<br>365   | gag<br>Glu        | aca<br>Thr        | gct<br>Ala        | gag<br>Glu        | gag<br>Glu<br>370 | ctg<br>Leu        | aag<br>Lys        | aag<br>Lys        | gtg<br>Val        | gct<br>Ala<br>375 | cag<br>G n        | gag<br>Glu        | ctg<br>Leu        | gag<br>Glu        | gag<br>Glu<br>380 | 1215 |
| aag<br>Lys          | cta<br>Leu        | aac<br>Asn        | att<br>He         | ctc<br>Leu<br>385 | aac<br>Asn        | aat<br>Asn        | aat<br>Asn        | tat<br>Tyr        | aag<br>Lys<br>390 | He                | ctg<br>Leu        | cag<br>G n        | gcg<br>Ala        | gac<br>Asp<br>395 | caa<br>Gln        | 1263 |
|                     | ctg<br>Leu        | tga               | ccac              | agg (             | gcag              | ggca              | gc c              | acca              | ggag              | a ga              | tatg              | cctg              | gca               | gggg              | сса               | 1319 |
| gga                 | caaa              | atg (             | caaa              | cttt              | tt t              | tttt              | tctg              | a ga              | caga              | gtct              | tgc               | tctg              | tcg               | ссаа              | gttgca            | 1379 |
| gtg                 | agcc              | gag               | atat              | cgcc              | ac t              | gcac              | tcca              | g cc              | tggg              | tgac              | aga               | gcga              | gac               | tcca              | tctcaa            | 1439 |
| aaa                 | aaaa              | aaa               | aaaa              | agaa              | ta t              | attg              | acgg              | a ag              | aata              | gaga              | gga               | ggct              | tga               | agga              | accagc            | 1499 |
| aat                 | gaga              | agg               | ccag              | gaaa              | ag a              | aaga              | gctg              | a aa              | atgg              | agaa              | agc               | ссаа              | gag               | ttag              | aacagt            | 1559 |

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<400> 121

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Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu 20 25 30

Asp Gly Lys Lys Phe Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys 35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val 50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr lle Ser Pro Asp 65 70 75 80

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| tcc cca gga gac ggg cgc acc ttc ccc aag cgc ggc cag acc tgc gtg  Ser Pro Gly Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val  10 15 20            |   |
| gtg cac tac acc ggg atg ctt gaa gat gga aag aaa ttt gat tcc tcc 208<br>Val His Tyr Thr Gly Met Leu Glu Asp Gly Lys Lys Phe Asp Ser Ser<br>25 30 35 40 |   |
| cgg gac aga aac aag ccc ttt aag ttt atg cta ggc aag cag gag gtg<br>Arg Asp Arg Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val<br>45 50 55        |   |
| atc cga ggc tgg gaa gaa ggg gtt gcc cag atg agt gtg ggt cag aga 304<br>lle Arg Gly Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg<br>60 65 70    |   |
| gcc aaa ctg act ata tct cca gat tat gcc tat ggt gcc act ggg cac Ala Lys Leu Thr lle Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His 75 80 85              |   |
| cca ggc atc atc cca cca cat gcc act ctc gtc ttc gat gtg gag ctt Pro Gly lle lle Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu 90 95 100             |   |
| cta aaa ctg gaa tgacaggaat ggcctcctcc cttagctccc tgttcttgga 452<br>Leu Lys Leu Glu<br>105   | - |
| tctgccatgg agggatctgg tgcctccaga catgtgcaca tgaatccata tggagctttt 512   |   |
| cctgatgttc cactccactt tgtatagaca tctgccctga ctgaatgtgt tctgtcactc 572   |   |
| agctttgctt ccgacacctc tgtttcctct tcccctttct cctcgtatgt gtgtttacct 632   |   |
| aaactatatg ccataaacct caagttactc attttatttt   |   |
| attcagtttc agtcttttgg atataggttt ccaattaagt acatggtcaa gtattaacag 752   |   |
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Phe Val Leu Ala Phe Ser Val Gly Ala Asn Asp Val Ala Asn Ser Phe 35 40 45

Gly Thr Ala Val Gly Ser Gly Val Val Thr Leu Lys Gln Ala Cys lle 50 55 60

Leu Ala Ser Ile Phe Glu Thr Val Gly Ser Val Leu Leu Gly Ala Lys 65 70 75 80

Val Ser Glu Thr lle Arg Lys Gly Leu lle Asp Val Glu Met Tyr Asn 85 90 95

Ser Thr Gln Gly Leu Leu Met Ala Gly Ser Val Ser Ala Met Phe Gly 100 105 110

Ser Ala Val Trp Gln Leu Val Ala Ser Phe Leu Lys Leu Pro Ile Ser 115 120 125

Gly Thr His Cys Ile Val Gly Ala Thr Ile Gly Phe Ser Leu Val Ala 130 135 140

Lys Gly Gln Glu Gly Val Lys Trp Ser Glu Leu lle Lys lle Val Met 145 150 155 160

Ser Trp Phe Val Ser Pro Leu Leu Ser Gly Ile Met Ser Gly Ile Leu 165 170 175

Phe Phe Leu Val Arg Ala Phe IIe Leu His Lys Ala Asp Pro Val Pro 180 185 190

Asn Gly Leu Arg Ala Leu Pro Val Phe Tyr Ala Cys Thr Val Gly !le



Asn Leu Phe Ser IIe Met Tyr Thr Gly Ala Pro Leu Leu Gly Phe Asp 210 215 220

Lys Leu Pro Leu Trp Gly Thr Ile Leu Ile Ser Val Gly Cys Ala Val 225 230 235 240

Phe Cys Ala Leu lle Val Trp Phe Phe Val Cys Pro Arg Met Lys Arg 245 250 255

Lys lle Glu Arg Glu lle Lys Cys Ser Pro Ser Glu Ser Pro Leu Met 260 265 270

Glu Lys Lys Asn Ser Leu Lys Glu Asp His Glu Glu Thr Lys Leu Ser 275 280 285

Val Gly Asp Ile Glu Asn Lys His Pro Val Ser Glu Val Gly Pro Ala 290 295 300

Thr Val Pro Leu Gln Ala Val Val Glu Glu Arg Thr Val Ser Phe Lys 305 310 315 320

Leu Gly Asp Leu Glu Glu Ala Pro Glu Arg Glu Arg Leu Pro Ser Val 325 330 335

Asp Leu Lys Glu Glu Thr Ser lle Asp Ser Thr Val Asn Gly Ala Val 340 345 350

Gin Leu Pro Asn Gly Asn Leu Val Gin Phe Ser Gin Ala Val Ser Asn 355 360 365

Gln lle Asn Ser Ser Gly His Tyr Gln Tyr His Thr Val His Lys Asp 370 375 380

Ser Gly Leu Tyr Lys Glu Leu Leu His Lys Leu His Leu Ala Lys Val 385 390 395 400

Gly Asp Cys Met Gly Asp Ser Gly Asp Lys Pro Leu Arg Arg Asn Asn 405 410 415

Ser Tyr Thr Ser Tyr Thr Met Ala IIe Cys Gly Met Pro Leu Asp Ser 420 425 430

Phe Arg Ala Lys Glu Glu Glu Glu Glu Glu Met Glu Lys Leu
435 440 445

Thr Trp Pro Asn Ala Asp Ser Lys Lys Arg IIe Arg Met Asp Ser Tyr 450 455 460

Thr Ser Tyr Cys Asn Ala Val Ser Asp Leu His Ser Ala Ser Glu IIe 465 470 475 480

Asp Met Ser Val Lys Ala Glu Met Gly Leu Gly Asp Arg Lys Gly Ser 485 490 495

Asn Gly Ser Leu Glu Glu Trp Tyr Asp Gln Asp Lys Pro Glu Val Ser 500 510

| Lot            | <i>a</i>                      | 515                | i                  | rne                      | Leu                        | um           | 520                |                    | inr          | Αιа          | Uys          | 525                | -                  | Ser          | Phe        |     |
|----------------|-------------------------------|--------------------|--------------------|--------------------------|----------------------------|--------------|--------------------|--------------------|--------------|--------------|--------------|--------------------|--------------------|--------------|------------|-----|
| Ala            | a His<br>530                  | Gly<br>)           | Gly                | Asn                      | Asp                        | Val<br>535   | Ser                | Asn                | Ala          | lle          | Gly<br>540   | Pro                | Leu                | Val          | Ala        |     |
| Leu<br>545     | ı Tyr                         | Leu                | Val                | Tyr                      | Asp<br>550                 | Thr          | Gly                | Asp                | Val          | Ser<br>555   | Ser          | Lys                | Val                | Ala          | Thr<br>560 |     |
| Pro            | lle                           | Trp                | Leu                | Leu<br>565               | Leu                        | Tyr          | Gly                | Gly                | Val<br>570   | Gly          | lle          | Cys                | Val                | Gly<br>575   | Leu        |     |
| Trp            | Val                           | Trp                | Gly<br>580         | Arg                      | Arg                        | Val          | lle                | Gln<br>585         | Thr          | Met          | Gly          | Lys                | Asp<br>590         | Leu          | Thr        |     |
| Pro            | lle                           | Thr<br>595         | Pro                | Ser                      | Ser                        | Gly          | Phe<br>600         | Ser                | lle          | Glu          | Leu          | Ala<br>605         | Ser                | Ala          | Leu        |     |
| Thr            | Val<br>610                    | Val                | He                 | Ala                      | Ser                        | Asn<br>615   | lle                | Gly                | Leu          | Pro          | lle<br>620   | Ser                | Thr                | Thr          | His        |     |
| Cys<br>625     | Lys                           | Val                | Gly                | Ser                      | Va l<br>630                | Val          | Ser                | Val                | Gly          | Trp<br>635   | Leu          | Arg                | Ser                | Lys          | Lys<br>640 |     |
| Ala            | Val                           | Asp                | Trp                | Arg<br>645               | Leu                        | Phe          | Arg                | Asn                | lle<br>650   | Phe          | Met          | Ala                |                    | Phe<br>655   | Val        |     |
| Thr            | Val                           | Pro                | lle<br>660         | Ser                      | Gly                        | Val          | lle                | Ser<br>665         | Ala          | Ala          | lle          |                    | Ala<br>670         | lle          | Phe        |     |
| Arg            | Tyr                           | Va I<br>675        | llel               | Leu ,                    | Arg 1                      | Met          |                    |                    |              |              |              |                    |                    |              |            |     |
| <211<br><212   | > 12<br>> 29<br>> DN<br>> Hor | 16<br>A            | apier              | าร                       |                            |              |                    |                    |              |              |              |                    |                    |              |            |     |
|                | ><br>> CD:<br>> (8            |                    | (2117              | <b>7</b> )               |                            |              |                    |                    |              |              |              |                    |                    |              |            |     |
| <4003<br>tttt  |                               |                    | cata               | ittot                    | gtt                        | taca         | ıcat               | cttg               | gaaag        | gc g         | ctca         | gtag               | st to              | tctt         | acta       | 60  |
|                |                               |                    |                    |                          | atg                        | gca          | ace                | cte                | att          | acc<br>Thr   | agt          | act                | aca                | gct          | gct        |     |
| acc g<br>Thr A | gcc g<br>Na A                 | ua S               | ct g<br>er G<br>15 | gt c<br>ly P             | ct t<br>ro L               | tg g<br>eu V | al A               | ac t<br>sp T<br>20 | ac c<br>yr L | ta t<br>eu T | gg a<br>rp M | et L               | tc a<br>eu l<br>25 | tc c<br>le L | tg<br>eu   | 161 |
| ggc t<br>Gly P | ne i                          | tt a<br>le l<br>30 | tt g<br>le A       | cat <sup>.</sup><br>IaPl | tt g <sup>.</sup><br>he Va | al Lo        | tg g<br>eu A<br>35 | ca t<br>Ia P       | tc to        | cc g<br>er V | al G         | ga g<br>iy A<br>40 | cc a<br>ia A       | at g<br>sn A | at<br>sp   | 209 |

|            |            |            |                   |            |            |            | gct               |                   |            |            |            |            |                   |            |            | 257 |
|------------|------------|------------|-------------------|------------|------------|------------|-------------------|-------------------|------------|------------|------------|------------|-------------------|------------|------------|-----|
| Val        | A!a<br>45  | Asn        | Ser               | Phe        | Gly        | Thr<br>50  | Ala               | Vai               | Gly        | Ser        | G∃y<br>55  | Val        | Val               | Thr        | Leu        |     |
|            |            |            |                   |            |            |            | agc<br>Ser        |                   |            |            |            |            |                   |            |            | 305 |
|            |            |            |                   |            |            |            | gaa<br>Glu        |                   |            |            |            |            |                   |            |            | 353 |
|            |            |            |                   |            |            |            | caa<br>Gln        |                   |            |            |            |            |                   |            |            | 401 |
|            |            |            |                   |            |            |            | gtg<br>Val<br>115 |                   |            |            |            |            |                   |            |            | 449 |
|            |            |            |                   |            |            |            | cat<br>His        |                   |            |            |            |            |                   |            |            | 497 |
|            |            |            |                   |            |            |            | cag<br>G n        |                   |            |            |            |            |                   |            |            | 545 |
|            |            |            |                   |            |            |            | ttc<br>Phe        |                   |            |            |            |            |                   |            |            | 593 |
| atg<br>Met | tct<br>Ser | gga<br>Gly | att<br>11e<br>175 | tta<br>Leu | ttc<br>Phe | ttc<br>Phe | ctg<br>Leu        | gtt<br>Val<br>180 | cgt<br>Arg | gca<br>Ala | ttc<br>Phe | atc<br>Ile | ctc<br>Leu<br>185 | cat<br>His | aag<br>Lys | 641 |
|            |            |            | Val               | Pro        | Asn        |            | ttg<br>Leu<br>195 |                   |            |            |            |            |                   |            |            | 689 |
|            |            |            |                   |            |            |            | ttt<br>Phe        |                   |            |            |            |            |                   |            |            | 737 |
|            |            |            |                   |            |            |            | cct<br>Pro        |                   |            |            |            |            |                   |            |            | 785 |
|            |            |            |                   |            |            |            | gcc<br>Ala        |                   |            |            |            |            |                   |            |            | 833 |
|            |            |            |                   |            |            |            | gaa<br>Glu        |                   |            |            |            |            |                   |            |            | 881 |
| gaa        | agc        | ccc        | tta               | atg        | gaa        | aaa        | aag               | aat               | agc        | ttg        | aaa        | gaa        | gac               | cat        | gaa        | 929 |

| Glu               | Ser               | Pro<br>270        | Leu                   | Met                  | <b>D</b> u        | Lys               | Lys<br>275        | Asn               | Ser               | Leu               | Lys               | G u<br>280        | A                 | lis               | Glu               |      |
|-------------------|-------------------|-------------------|-----------------------|----------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| gaa<br>Glu        | aca<br>Thr<br>285 | aag<br>Lys        | ttg<br>Leu            | tct<br>Ser           | gtt<br>Val        | ggt<br>Gly<br>290 | gat<br>Asp        | att<br>lle        | gaa<br>Glu        | aac<br>Asn        | aag<br>Lys<br>295 | cat<br>His        | cct<br>Pro        | gtt<br>Val        | tct<br>Ser        | 977  |
| gag<br>Glu<br>300 | gta<br>Val        | ggg<br>Gly        | cct<br>Pro            | gcc<br>Ala           | act<br>Thr<br>305 | gtg<br>Val        | ccc<br>Pro        | ctc<br>Leu        | cag<br>Gln        | gct<br>Ala<br>310 | gtg<br>Val        | gtg<br>Val        | gag<br>Glu        | gag<br>Glu        | aga<br>Arg<br>315 | 1025 |
| aca<br>Thr        | gtc<br>Val        | tca<br>Ser        | ttc<br>Phe            | aaa<br>Lys<br>320    | ctt<br>Leu        | gga<br>Gly        | gat<br>Asp        | ttg<br>Leu        | gag<br>Glu<br>325 | gaa<br>Glu        | gct<br>Ala        | cca<br>Pro        | gag<br>Glu        | aga<br>Arg<br>330 | gag<br>Glu        | 1073 |
| agg<br>Arg        | ctt<br>Leu        | ccc<br>Pro        | agc<br>Ser<br>335     | gtg<br>Val           | gac<br>Asp        | ttg<br>Leu        | aaa<br>Lys        | gag<br>Glu<br>340 | gaa<br>Glu        | acc<br>Thr        | agc<br>Ser        | ata<br>Ile        | gat<br>Asp<br>345 | agc<br>Ser        | acc<br>Thr        | 1121 |
| gtg<br>Val        | aat<br>Asn        | ggt<br>Gly<br>350 | gca<br>Ala            | gtg<br>Val           | cag<br>Gln        | ttg<br>Leu        | cct<br>Pro<br>355 | aat<br>Asn        | ggg<br>Gly        | aac<br>Asn        | ctt<br>Leu        | gtc<br>Val<br>360 | cag<br>Gln        | ttc<br>Phe        | agt<br>Ser        | 1169 |
| caa<br>Gln        | gcc<br>Ala<br>365 | gtc<br>Val        | agc<br>Ser            | aac<br>Asn           | caa<br>Gln        | ata<br>  e<br>370 | aac<br>Asn        | tcc<br>Ser        | agt<br>Ser        | ggc<br>Gly        | cac<br>His<br>375 | tac<br>Tyr        | cag<br>G n        | tat<br>Tyr        | cac<br>His        | 1217 |
| acc<br>Thr<br>380 | Val               | cat<br>His        | aag<br>Lys            | gat<br>Asp           | tcc<br>Ser<br>385 | ggc<br>Gly        | ctg<br>Leu        | tac<br>Tyr        | aaa<br>Lys        | gag<br>Glu<br>390 | cta<br>Leu        | ctc<br>Leu        | cat<br>His        | aaa<br>Lys        | tta<br>Leu<br>395 | 1265 |
| cat<br>His        | ctt<br>Leu        | gcc<br>Ala        | aag<br>Lys            | gtg<br>Val<br>400    | gga<br>Gly        | gat<br>Asp        | tgc<br>Cys        | atg<br>Met        | gga<br>Gly<br>405 | gac<br>Asp        | tcc<br>Ser        | ggt<br>Gly        | gac<br>Asp        | aaa<br>Lys<br>410 | Pro               | 1313 |
| tta<br>Leu        | agg<br>Arg        | cgc<br>Arg        | aat<br>Asn<br>415     | aat<br>Asn           | agc<br>Ser        | tat<br>Tyr        | act<br>Thr        | tcc<br>Ser<br>420 | Tyr               | acc<br>Thr        | atg<br>Met        | gca<br>Ala        | ata<br>Ile<br>425 | tgt<br>Cys        | ggc<br>Gly        | 1361 |
| atg<br>Met        | cct<br>Pro        | ctg<br>Leu<br>430 | Asp                   | tca<br>Ser           | ttc<br>Phe        | cgt<br>Arg        | gcc<br>Ala<br>435 | Lys               | gaa<br>Glu        | ggt<br>Gly        | gaa<br>Glu        | cag<br>Gln<br>440 | Lys               | ggc<br>Gly        | gaa<br>Glu        | 1409 |
| gaa<br>Glu        | atg<br>Met<br>445 | Glu               | aag<br>Lys            | ctg<br>Leu           | aca<br>Thr        | tgg<br>Trp<br>450 | Pro               | aat<br>Asn        | gca<br>Ala        | gac<br>Asp        | tco<br>Ser<br>455 | Lys               | aag<br>Lys        | cga<br>Arg        | att<br>; lle      | 1457 |
| cga<br>Arg<br>460 | Met               | g gac<br>: Asp    | agt<br>Ser            | tac<br>Tyr           | acc<br>Thr<br>465 | Ser               | tac<br>Tyr        | tgc<br>Cys        | aat<br>Asn        | gct<br>Ala<br>470 | ı Val             | g tot<br>Ser      | gac<br>Asp        | ctt<br>Leu        | cac<br>His<br>475 | 1505 |
| tca<br>Ser        | gca<br>Ala        | tct<br>Ser        | gag<br>Glu            | g ata<br>ılle<br>480 | : Asp             | atg<br>Met        | g agt<br>: Ser    | gtc<br>Val        | aag<br>Lys<br>485 | Ala               | a gag<br>a Glu    | g atg<br>ı Met    | g ggt<br>Gly      | cta<br>Leu<br>490 | ggt<br>Gly        | 1553 |
| gac<br>Asp        | aga<br>Arg        | a aaa<br>g Lys    | a gga<br>s Gly<br>495 | / Ser                | aat<br>Asr        | ggc<br>Gly        | c tct<br>/ Ser    | cta<br>Leu<br>500 | ı Glu             | a gaa<br>u Glu    | a tgg<br>i Trp    | g tat<br>o Tyr    | gac<br>Asp<br>505 | Glr               | g gat<br>n Asp    | 1601 |

| aag cct gaa gtc tct etc ctc ttc cag ttc ctg cag atc ctt aca gcc Lys Pro Glu Val Ser Leu Leu Phe Gln Phe Leu Gln Ile Leu Thr Ala 510 515 520                | }   |
|--|-----|
| tgc ttt ggg tca ttc gcc cat ggt ggc aat gac gta agc aat gcc att 1697<br>Cys Phe Gly Ser Phe Ala His Gly Gly Asn Asp Val Ser Asn Ala Ile<br>525 530 535     | 7   |
| ggg cct ctg gtt gct tta tat ttg gtt tat gac aca gga gat gtt tct 1745<br>Gly Pro Leu Val Ala Leu Tyr Leu Val Tyr Asp Thr Gly Asp Val Ser<br>540 545 550 555 | 5   |
| tca aaa gtg gca aca cca ata tgg ctt cta ctc tat ggt ggt gtt ggt 1793<br>Ser Lys Val Ala Thr Pro Ile Trp Leu Leu Leu Tyr Gly Gly Val Gly<br>560 565 570     | 3   |
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| ggg aag gat ctg aca ccg atc aca ccc tct agt ggc ttc agt att gaa 1889<br>Gly Lys Asp Leu Thr Pro lle Thr Pro Ser Ser Gly Phe Ser lle Glu<br>590 595 600     | Э   |
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| ctc cgg tcc aag aag gct gtt gac tgg cgt ctc ttt cgt aac att ttt 2033<br>Leu Arg Ser Lys Lys Ala Val Asp Trp Arg Leu Phe Arg Asn Ile Phe<br>640 645 650     | 3   |
| atg gcc tgg ttt gtc aca gtc cct att tct gga gtt atc agt gct gcc 2081<br>Met Ala Trp Phe Val Thr Val Pro lle Ser Gly Val lle Ser Ala Ala<br>655 660 665     | 1   |
| atc atg gca atc ttc aga tat gtc atc ctc aga atg tgaagctgtt 2127<br>lle Met Ala lle Phe Arg Tyr Val lle Leu Arg Met<br>670 675                              | 7   |
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ttaaatggga cagccttcca tgttcatttg tctacctctt aactgaataa aaaagcctac 2907
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<211> 288

<212> PRT

<213> Homo sapiens

<400> 125

Met Glu Arg Pro Gln Pro Asp Ser Met Pro Gln Asp Leu Ser Glu Ala 1 5 10 15

Leu Lys Glu Ala Thr Lys Glu Val His Thr Gln Ala Glu Asn Ala Glu 20 25 30

Phe Met Arg Asn Phe Gln Lys Gly Gln Val Thr Arg Asp Gly Phe Lys 35 40 45

Leu Val Met Ala Ser Leu Tyr His Ile Tyr Val Ala Leu Glu Glu Glu 50 55 60

lle Glu Arg Asn Lys Glu Ser Pro Val Phe Ala Pro Val Tyr Phe Pro 65 70 75 80

Glu Glu Leu His Arg Lys Ala Ala Leu Glu Gln Asp Leu Ala Phe Trp 85 90 95

Tyr Gly Pro Arg Trp Gln Glu Val lle Pro Tyr Thr Pro Ala Met Gln 100 105 110

Arg Tyr Val Lys Arg Leu His Glu Val Gly Arg Thr Glu Pro Glu Leu 115 120 125

Leu Val Ala His Ala Tyr Thr Arg Tyr Leu Gly Asp Leu Ser Gly Gly 130 135 140

Gln Val Leu Lys Lys Ile Ala Gln Lys Ala Leu Asp Leu Pro Ser Ser 145 150 155 160

Gly Glu Gly Leu Ala Phe Phe Thr Phe Pro Asn Ile Ala Ser Ala Thr 165 170 175

Lys Phe Lys Gln Leu Tyr Arg Ser Arg Met Asn Ser Leu Glu Met Thr 180 185 190

| Pro  | Ala   | Val<br>195                                   | Arg  | GI   | g   | Val   | lle<br>200   | G∣u  | Glu  | Ala   | Lys  | Thr<br>205                                   |  | Phe  | Leu   |   |
|--|---|--|--|--|---|---|--|--|--|---|--|--|--|--|---|---|
| Leu  | Asn<br>210  | He   | Gln  | Leu  | Phe   | Glu<br>215  | Głu  | Leu  | Gln  | Glu   | Leu<br>220   | Leu  | Thr  | His  | Asp   |   |
| Thr<br>225   | Lys   | Asp  | Gln  | Ser  | Pro<br>230  | Ser   | Arg  | Ala  | Pro  | Gly<br>235  | Leu  | Arg  | Gln  | Arg  | Ala<br>240  |   |
| Ser  | Asn   | Lys  | Val  | GIn<br>245   | Asp   | Ser   | Ala  | Pro  | Val<br>250   | Glu   | Thr  | Pro  | Arg  | Gly<br>255   | Lys   |   |
| Pro  | Pro   | Leu  | Asn<br>260   | Thr  | Arg   | Ser   | Gln  | Ala<br>265   | Pro  | Leu   | Leu  | Arg  | Trp<br>270                                   | Val  | Leu   |   |
| Thr  | Leu   | Ser<br>275                                   | Phe  | Leu  | Val   | Ala   | Thr<br>280   | Val  | Ala  | Val   | Gly  | Leu<br>285                                   | Tyr  | Ala  | Met   |   |
| <211<br><212   | 210> 126<br>211> 1550<br>212> DNA<br>213> Homo sapiens                        |  |  |  |   |   |  |  |  |   |  |  |  |  |   |   |
| <221   | (220)<br>(221) CDS<br>(222) (81)(944)   |  |  |  |   |   |  |  |  |   |  |  |  |  |   |   |
| / 400  | <400> 126 tcaacgcctg cctcccctcg agcgtcctca gcgcagccgc cgcccgcgga gccagcacga 6 |  |  |  |   |   |  |  |  |   |  |  |  |  |   |   |
|  |   |  | ctc  | ccto   | cg ag   | gcgto   | cctca  | a gc   | gcago  | ccgc  | cgc  | cgce   | gga g  | gccag  | gcacga  | 60  |
| tcaa   | acgco   | ctg c  |  |  | ggjat   | tg ga   | ag cg  | gt co  | og ca  | аа со   | cc ga  | ac ag  | gc at  | tg co  | gcacga<br>cc cag<br>co Gln                            |   |
| tcaa<br>acga<br>gat  | acgco<br>agcco<br>ttg   | ctg constant                                 | gag  | ggccg  | gg_at<br>Me   | tg ga<br>et Gl  | ag cg<br>Iu Ar<br>gag                              | gt co<br>rg Pr<br>gcc                                      | og ca<br>o G   | aa co<br>In Pr<br>5<br>aag  | cc garon As  | ac ag<br>sp Se<br>gtg                        | gc at<br>er Me                               | ig co<br>et Pr<br>acc                                | cc cag<br>co Gln<br>lO<br>cag                         |   |
| acga<br>gat<br>Asp   | acgco<br>agcco<br>ttg<br>Leu<br>gag   | cag o<br>tca<br>Ser                          | gag<br>Glu<br>15   | gcc<br>gcc<br>Ala<br>gag   | gg at<br>Me<br>ctg<br>Leu<br>ttc                                  | tg ga<br>et Gl<br>1<br>aag  | ag cg<br>lu Ar<br>gag<br>Glu<br>agg                | gt co<br>rg Pr<br>gcc<br>Ala<br>20<br>aac                  | og ca<br>ro G<br>acc<br>Thr                          | aa co<br>In Pr<br>5<br>aag<br>Lys   | gag<br>Glu   | gtg<br>Val                                   | gc at<br>er Me<br>cac<br>His<br>25           | acc<br>Thr   | cc cag<br>o Gln<br>lO<br>cag<br>Gln                   | 113   |
| gat<br>Asp<br>gca<br>Ala                                   | ttg<br>Leu<br>gag<br>Glu  | tca<br>Ser<br>aat<br>Asn<br>30               | gag<br>Glu<br>15<br>gct<br>Ala                             | gcc<br>gcc<br>Ala<br>gag<br>Glu<br>aag                             | gg at<br>Me<br>ctg<br>Leu<br>ttc<br>Phe                           | tg ga<br>et G<br>1<br>aag<br>Lys  | gag<br>Glu<br>agg<br>Arg<br>35                     | gt co<br>gcc<br>Ala<br>20<br>aac<br>Asn                    | acc<br>Thr<br>ttt<br>Phe                             | aa co<br>in Pr<br>5<br>aag<br>Lys<br>cag<br>GIn                                   | gag<br>Glu<br>aag<br>Lys                                   | gtg<br>Val<br>ggc<br>Gly<br>40               | cac<br>His<br>25<br>cag<br>Gln               | acc<br>Thr<br>gtg<br>Val                             | cag<br>Gln<br>acc<br>Thr                              | 113   |
| gat<br>Asp<br>gca<br>Ala<br>cga<br>Arg                     | ttg<br>Leu<br>gag<br>Glu<br>gac<br>Asp<br>45                                  | tca<br>Ser<br>aat<br>Asn<br>30<br>ggc<br>Gly | gag<br>Glu<br>15<br>gct<br>Ala<br>ttc<br>Phe               | gcc<br>Ala<br>gag<br>Glu<br>aag<br>Lys                             | gg at Me ctg Leu ttc Phe ctg Leu att                              | tg ga<br>et G<br>1<br>aag<br>Lys<br>atg<br>Met                            | gag<br>Glu<br>agg<br>Arg<br>35<br>atg<br>Met       | gt co<br>gcc<br>Ala<br>20<br>aac<br>Asn<br>gcc<br>Ala      | acc<br>Thr<br>ttt<br>Phe<br>tcc<br>Ser               | aa co<br>in Pr<br>5<br>aag<br>Lys<br>cag<br>GIn<br>ctg<br>Leu                     | gag<br>Glu<br>aag<br>Lys<br>tac<br>Tyr<br>55               | gtg<br>Val<br>ggc<br>Gly<br>40<br>cac<br>His | cac<br>His<br>25<br>cag<br>Gln<br>atc        | acc<br>Thr<br>gtg<br>Val<br>tat<br>Tyr               | cc cag o Gln o cag Gln acc Thr gtg Val                | <ul><li>113</li><li>161</li><li>209</li></ul>             |
| gat<br>Asp<br>gca<br>Ala<br>cga<br>Arg<br>gcc<br>Ala<br>60 | ttg<br>Leu<br>gag<br>Glu<br>gac<br>Asp<br>ctg<br>Leu                          | tca<br>Ser<br>aat<br>Asn<br>30<br>ggc<br>Gly | gag<br>Glu<br>15<br>gct<br>Ala<br>ttc<br>Phe<br>gag<br>Glu | gcc<br>gcc<br>Ala<br>gag<br>Glu<br>aag<br>Lys<br>gag<br>Glu<br>cca | ctg<br>Leu<br>ttc<br>Phe<br>ctg<br>Leu<br>att<br>11e<br>65<br>gaa | tg ga<br>et G<br>1<br>aag<br>Lys<br>atg<br>Met<br>gtg<br>Val<br>50<br>gag | ag callu Argaggaguaggagagagagagagagagagagagagagaga | gcc<br>Ala<br>20<br>aac<br>Asn<br>gcc<br>Ala<br>aac<br>Asn | acc<br>Thr<br>ttt<br>Phe<br>tcc<br>Ser<br>aag<br>Lys | aa co<br>In Pr<br>5<br>aag<br>Lys<br>cag<br>GIn<br>ctg<br>Leu<br>gag<br>Glu<br>70 | gag<br>Glu<br>aag<br>Lys<br>tac<br>Tyr<br>55<br>agc<br>Ser | gtg<br>Val<br>ggc<br>Gly<br>40<br>cac<br>His | cac<br>His<br>25<br>Cag<br>Gln<br>atc<br>Ile | acc<br>Thr<br>gtg<br>Val<br>tat<br>Tyr<br>ttc<br>Phe | cc cag o Gln o cag Gln acc Thr gtg Val gcc Ala 75 cag | <ul><li>113</li><li>161</li><li>209</li><li>257</li></ul> |

| aca cca gcc atg cag egc tat gtg aag cgg ctc cac gag gtg ggg cgc Thr Pro Ala Met Gin Arg Tyr Val Lys Arg Leu His Glu Val Gly Arg 110 115 120          | 9         |
|--|-----------|
| aca gag ccc gag ctg ctg gtg gcc cac gcc tac acc cgc tac ctg ggt 49 Thr Glu Pro Glu Leu Leu Val Ala His Ala Tyr Thr Arg Tyr Leu Gly 125 130 135       | 7         |
| gac ctg tct ggg ggc cag gtg ctc aaa aag att gcc cag aaa gcc ctg Asp Leu Ser Gly Gly Gln Val Leu Lys Lys lle Ala Gln Lys Ala Leu 140 145 150 155      | 5         |
| gac ctg ccc agc tct ggc gag ggc ctg gcc ttc ttc acc ttc ccc aac  Asp Leu Pro Ser Ser Gly Glu Gly Leu Ala Phe Phe Thr Phe Pro Asn  160 165 170        | <b>,3</b> |
| att gcc agt gcc acc aag ttc aag cag ctc tac cgc tcc cgc atg aac 64<br>lle Ala Ser Ala Thr Lys Phe Lys Gln Leu Tyr Arg Ser Arg Met Asn<br>175 180 185 | ,1        |
| tcc ctg gag atg act ccc gca gtc agg cag agg gtg ata gaa gag gcc 68<br>Ser Leu Glu Met Thr Pro Ala Val Arg Gln Arg Val Ile Glu Glu Ala<br>190 195 200 | 19        |
| aag act gcg ttc ctg ctc aac atc cag ctc ttt gag gag ttg cag gag<br>Lys Thr Ala Phe Leu Leu Asn Ile Gln Leu Phe Glu Glu Leu Gln Glu<br>205 210 215    | 37        |
| ctg ctg acc cat gac acc aag gac cag agc ccc tca cgg gca cca ggg Leu Leu Thr His Asp Thr Lys Asp Gln Ser Pro Ser Arg Ala Pro Gly 220 225 230 235      | 35 .      |
| ctt cgc cag cgg gcc agc aac aaa gtg caa gat tct gcc ccc gtg gag 83<br>Leu Arg Gln Arg Ala Ser Asn Lys Val Gln Asp Ser Ala Pro Val Glu<br>240 245 250 | 13        |
| act ccc aga ggg aag ccc cca ctc aac acc cgc tcc cag gct ccg ctt 88<br>Thr Pro Arg Gly Lys Pro Pro Leu Asn Thr Arg Ser Gln Ala Pro Leu<br>255 260 265 | 31        |
| ctc cga tgg gtc ctt aca ctc agc ttt ctg gtg gcg aca gtt gct gta 92<br>Leu Arg Trp Val Leu Thr Leu Ser Phe Leu Val Ala Thr Val Ala Val<br>270 275 280 | 29        |
| ggg ctt tat gcc atg tgaatgcagg catgctggct cccagggcca tgaactttgt 98<br>Gly Leu Tyr Ala Met<br>285   | 34        |
| ccggtggaag gccttctttc tagagaggga attctcttgg ctggcttcct taccgtgggc 10   | )44       |
| actgaagget ttcagggeet ccagecetet caetgtgtee etetetetgg aaaggaggaa 11   | 104       |
| ggagcctatg gcatcttccc caacgaaaag cacatccagg caatggccta aacttcagag 11   | 164       |
| ggggcgaagg ggtcagccct gcccttcagc atcctcagtt cctgcagcag agcctggaag 12   | 224       |
| acaccctaat gtggcagctg tctcaaacct ccaaaagccc tgagtttcaa gtatccttgt 12   | 284       |

tgacacggcc atgaccactt tccccgtggg ccatggcaat ttttacacaa acctgaaaag 1344
atgttgtgtc ttgtgttttt gtcttatttt tgttggagcc actctgttcc tggctcagcc 1404
tcaaatgcag tattttgtt gtgttctgtt gttttatag cagggttggg gtggttttt 1464
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<210> 127

<211> 135 <212> PRT

<213> Homo sapiens

<400> 127

Met Ala Cys Gly Leu Val Ala Ser Asn Leu Asn Leu Lys Pro Gly Glu
1 5 10 15

Cys Leu Arg Val Arg Gly Glu Val Ala Pro Asp Ala Lys Ser Phe Val 20 25 30

Leu Asn Leu Gly Lys Asp Ser Asn Asn Leu Cys Leu His Phe Asn Pro 35 40 45

Arg Phe Asn Ala His Gly Asp Ala Asn Thr Ile Val Cys Asn Ser Lys 50 55 60

Asp Gly Gly Ala Trp Gly Thr Glu Gln Arg Glu Ala Val Phe Pro Phe 65 70 75 80

Gln Pro Gly Ser Val Ala Glu Val Cys lle Thr Phe Asp Gln Ala Asn 85 90 95

Leu Thr Val Lys Leu Pro Asp Gly Tyr Glu Phe Lys Phe Pro Asn Arg 100 105 110

Leu Asn Leu Glu Ala Ile Asn Tyr Met Ala Ala Asp Gly Asp Phe Lys 115 120 125

lle Lys Cys Val Ala Phe Asp 130 135

<210> 128

<211> 507

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (50).. (454)

<400> 128

cttctgacag ctggtgcgcc tgcccgggaa catcctcctg gactcaatc atg gct tgt 58

Met Ala Cys

|  |                  | ı Asn Leu Lys       | cct gga gag tgc ctt cga<br>Pro Gly Glu Cys Leu Arg<br>15    | 106 |
|--|------------------|---------------------|---|-----|
|  |                  |                     | agc ttc gtg ctg aac ctg<br>Ser Phe Val Leu Asn Leu<br>30 35 | 154 |
|  |                  |                     | ttc aac cct cgc ttc aac<br>Phe Asn Pro Arg Phe Asn<br>50    | 202 |
|  |                  |                     | aac agc aag gac ggc ggg<br>Asn Ser Lys Asp Gly Gly<br>65    | 250 |
|  |                  |                     | ttt ccc ttc cag cct gga<br>Phe Pro Phe Gln Pro Gly<br>80    | 298 |
|  |                  | Thr Phe Asp         | cag gcc aac ctg acc gtc<br>Gln Ala Asn Leu Thr Val<br>95    | 346 |
|  |                  |                     | ccc aac cgc ctc aac ctg<br>Pro Asn Arg Leu Asn Leu<br>110   | 394 |
|  |                  |                     | gac ttc aag atc aaa tgt<br>Asp Phe Lys IIe Lys Cys<br>130   | 442 |
| gtg gcc ttt gac<br>Val Ala Phe Asp<br>135              | tgaaatcagc       | cagcccatgg c        | ccccaataa aggcagctgc  | 494 |
| ctctgctccc ctg   |                  |                     |   | 507 |
| <210> 129<br><211> 662<br><212> PRT<br><213> Homo sapi | ens              |                     |   |     |
| <400> 129<br>Met Asn Lys Glu<br>1                      | lle Pro Asr<br>5 | ı Gly Asn Thr<br>10 | Ser Glu Leu IIe Phe Asn<br>15                               |     |
| Ala Val His Val  | Lys Asp Ala      | Gly Phe Tyr<br>25   | Val Cys Arg Val Asn Asn<br>30                               |     |
| Asn Phe Thr Phe  | Glu Phe Ser      | Gln Trp Ser<br>40   | Gln Leu Asp Val Cys Asp<br>45                               |     |
| lle Pro Glu Ser<br>50                                  | Phe Gln Arg      |                     | Gly Val Ser Glu Ser Lys<br>60                               |     |

Leu Gln lle Cys Val Glu Pro Thr Ser Gln Lys Leu Met Pro Gly Ser Thr Leu Val Leu Gln Cys Val Ala Val Gly Ser Pro Ile Pro His Tyr Gln Trp Phe Lys Asn Glu Leu Pro Leu Thr His Glu Thr Lys Lys Leu 105 Tyr Met Val Pro Tyr Val Asp Leu Glu His Gln Gly Thr Tyr Trp Cys His Val Tyr Asn Asp Arg Asp Ser Gln Asp Ser Lys Lys Val Glu lle lle lle Gly Arg Thr Asp Glu Ala Val Glu Cys Thr Glu Asp Glu Leu Asn Asn Leu Gly His Pro Asp Asn Lys Glu Gln Thr Thr Asp Gln Pro Leu Ala Lys Asp Lys Val Ala Leu Leu lle Gly Asn Met Asn Tyr Arg Glu His Pro Lys Leu Lys Ala Pro Leu Val Asp Val Tyr Glu Leu Thr Asn Leu Leu Arg Gin Leu Asp Phe Lys Val Val Ser Leu Leu Asp Leu Thr Glu Tyr Glu Met Arg Asn Ala Val Asp Glu Phe Leu Leu Leu 235 240 Asp Lys Gly Val Tyr Gly Leu Leu Tyr Tyr Ala Gly His Gly Tyr Glu Asn Phe Gly Asn Ser Phe Met Val Pro Val Asp Ala Pro Asn Pro Tyr 265 Arg Ser Glu Asn Cys Leu Cys Val Gln Asn lle Leu Lys Leu Met Gln Glu Lys Glu Thr Gly Leu Asn Val Phe Leu Leu Asp Met Cys Arg Lys 295 Arg Asn Asp Tyr Asp Asp Thr lie Pro Ile Leu Asp Ala Leu Lys Vai 320

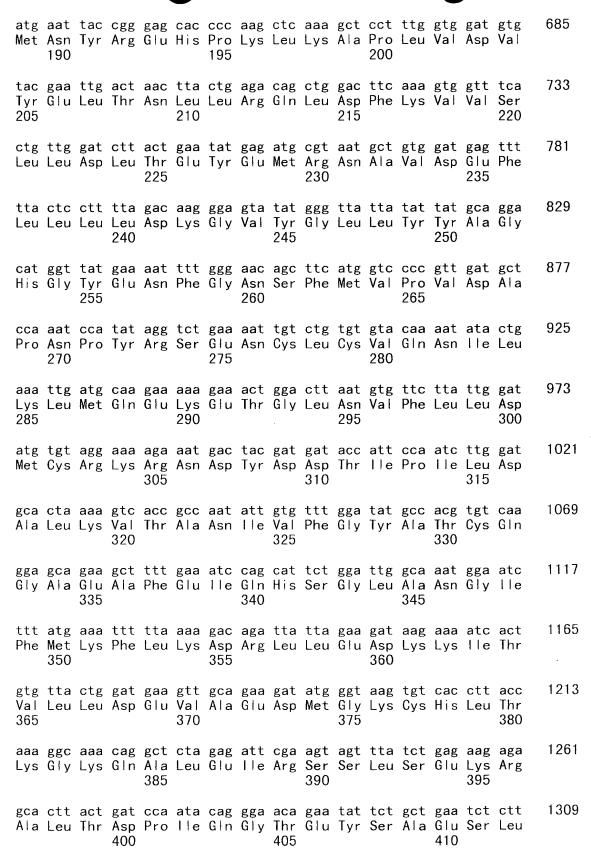
Thr Ala Asn lle Val Phe Gly Tyr Ala Thr Cys Gln Gly Ala Glu Ala 330

Phe Glu lle Gln His Ser Gly Leu Ala Asn Gly lle Phe Met Lys Phe 340

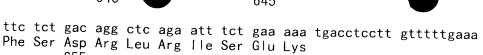
Leu Lys Asp Arg Leu Leu Glu Asp Lys lle Thr Val Leu Leu Asp 355 360

| G١          | u Va<br>370 | l Al       | a Gl         | u As         | et          | Gly<br>375 | / Lys      | s Cys      | s His      | s Lei        | 1 Thr<br>380 |            |            | Lys        | s Glr      |
|-------------|-------------|------------|--------------|--------------|-------------|------------|------------|------------|------------|--------------|--------------|------------|------------|------------|------------|
| A1<br>38    | a Lei<br>5  | u Gl       | u H          | e Arg        | 390         | Ser        | Leu        | ı Sei      | Glu        | 1 Lys<br>395 | s Arg        | g Ala      | a Lei      | ı Thr      | 400        |
| Pro         | o lle       | e GI       | n Gl         | y Thr<br>405 | Glu         | Tyr        | Ser        | Ala        | 410        |              | Leu          | ı Val      | Arg        | 415        |            |
| Gli         | n Trp       | A L        | a Lys<br>420 | s Ala        | a His       | Glu        | ı Leu      | Pro<br>425 |            | Ser          | Met          | Cys        | Leu<br>430 |            | Phe        |
| Asp         | Cys         | 43         | y Va<br>5    | l Gir        | ılle        | Gin        | Leu<br>440 | Gly        | Phe        | Ala          | Ala          | Glu<br>445 |            | . Ser      | Asn        |
| Val         | Met<br>450  | . 116      | e lle        | e Tyr        | Thr         | Ser<br>455 | He         | Val        | Tyr        | Lys          | Pro<br>460   |            | Glu        | ılle       | lle        |
| Met<br>465  | Cys         | Asp        | o Ala        | a Tyr        | Va l<br>470 | Thr        | Asp        | Phe        | Pro        | Leu<br>475   |              | Leu        | Asp        | lle        | Asp<br>480 |
| Pro         | Lys         | Asp        | o Ala        | 485          | Lys         | Gly        | Thr        | Pro        | Glu<br>490 | Glu          | Thr          | Gly        | Ser        | Tyr<br>495 |            |
| Val         | Ser         | Lys        | 500          | Leu<br>I     | Pro         | Lys        | His        | Cys<br>505 | Leu        | Tyr          | Thr          | Arg        | Leu<br>510 | Ser        | Ser        |
| Leu         | Gln         | Lys<br>515 | Leu          | Lys          | Glu         | His        | Leu<br>520 | Val        | Phe        | Thr          | Val          | Cys<br>525 | Leu        | Ser        | Tyr        |
| GIn         | Tyr<br>530  | Ser        | Gly          | Leu          | Glu         | Asp<br>535 | Thr        | Val        | Glu        | Asp          | Lys<br>540   | Gln        | Glu        | Val        | Asn        |
| Va I<br>545 | Gly         | Lys        | Pro          | Leu          | 11e<br>550  | Ala        | Lys        | Leu        | Asp        | Met<br>555   | His          | Arg        | Gly        | Leu        | Gly<br>560 |
| Arg         | Lys         | Thr        | Cys          | Phe<br>565   | Gln         | Thr        | Cys        | Leu        | Met<br>570 | Ser          | Asn          | Gly        | Pro        | Tyr<br>575 | Gln        |
| Ser         | Ser         | Ala        | Ala<br>580   | Thr          | Ser         | Gly        | Gly        | Ala<br>585 | Gly        | His          | Tyr          | His        | Ser<br>590 | Leu        | Gln        |
| Asp         | Pro         | Phe<br>595 | His          | Gly          | Val         | Tyr        | His<br>600 | Ser        | His        | Pro          | Gly          | Asn<br>605 | Pro        | Ser        | Asn        |
| Val         | Thr<br>610  | Pro        | Ala          | Asp          |             | Cys<br>615 | His        | Cys        | Ser        | Arg          | Thr<br>620   | Pro        | Asp        | Ala        | Phe        |
| 11e<br>625  | Ser         | Ser        | Phe          | Ala          | His<br>630  | His        | Ala        | Ser        | Cys        | His<br>635   | Phe          | Ser        | Arg        | Ser        | Asn<br>640 |
| Val         | Pro         | Val        | Glu          | Thr<br>645   | Thr         | Asp        | Glu        | lle        | Pro<br>650 | Phe          | Ser          | Phe        | Ser        | Asp<br>655 | Arg        |
| Leu         | Arg         | He         | Ser<br>660   | Glu          | Lys         |            |            |            |            |              |              |            |            |            |            |

| <210> 130<br><211> 2251<br><212> DNA<br><213> Homo sapiens  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| <220><br><221> CDS<br><222> (74) (2059)   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| <400> 130 cttggctgga cagtttgtga aactgtgttg ccgggcaact ggacatcctt ttgttcaata 60  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| tcagtggttc aaa atg aat aaa gag att cca aat gga aat aca tca gag 109<br>Met Asn Lys Glu lle Pro Asn Gly Asn Thr Ser Glu<br>1 5 10                       |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| ctt att ttt aat gca gtg cat gta aaa gat gca ggc ttt tat gtc tgt 157<br>Leu IIe Phe Asn Ala Val His Val Lys Asp Ala Gly Phe Tyr Val Cys<br>15 20 25    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| cga gtt aat aac aat ttc acc ttt gaa ttc agc cag tgg tca cag ctg 205<br>Arg Val Asn Asn Asn Phe Thr Phe Glu Phe Ser Gln Trp Ser Gln Leu<br>30 35 40    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| gat gtt tgc gac atc cca gag agc ttc cag aga agt gtt gat ggc gtc 253<br>Asp Val Cys Asp lle Pro Glu Ser Phe Gln Arg Ser Val Asp Gly Val<br>45 50 55 60 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| tct gaa tcc aag ttg caa atc tgt gtt gaa cca act tcc caa aag ctg 301<br>Ser Glu Ser Lys Leu Gln 11e Cys Val Glu Pro Thr Ser Gln Lys Leu<br>65 70 75    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| atg cca ggc agc aca ttg gtt tta cag tgt gtt gct gtt gga agc cct 349<br>Met Pro Gly Ser Thr Leu Val Leu Gln Cys Val Ala Val Gly Ser Pro<br>80 85 90    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| att cct cac tac cag tgg ttc aaa aat gaa tta cca tta aca cat gag 397<br>Ile Pro His Tyr Gln Trp Phe Lys Asn Glu Leu Pro Leu Thr His Glu<br>95 100 105  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| acc aaa aag cta tac atg gtg cct tat gtg gat ttg gaa cac caa gga 445 Thr Lys Lys Leu Tyr Met Val Pro Tyr Val Asp Leu Glu His Gln Gly 110 115 120       |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| acc tac tgg tgt cat gta tat aat gat cga gac agt caa gat agc aag Thr Tyr Trp Cys His Val Tyr Asn Asp Arg Asp Ser Gln Asp Ser Lys 125 130 135 140       |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| aag gta gaa atc atc ata gga aga aca gat gag gca gtg gag tgc act 541<br>Lys Val Glu lle lle Gly Arg Thr Asp Glu Ala Val Glu Cys Thr<br>145 150 155     |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| gaa gat gaa tta aat aat ctt ggt cat cct gat aat aaa gag caa aca 589<br>Glu Asp Glu Leu Asn Asn Leu Gly His Pro Asp Asn Lys Glu Gln Thr<br>160 165 170 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| act gac cag cct ttg gcg aag gac aag gtt gcc ctt ttg ata gga aat 637<br>Thr Asp Gin Pro Leu Ala Lys Asp Lys Val Ala Leu Leu Ile Gly Asn                |  |  |  |  |  |  |  |  |  |  |  |  |  |  |



| gtg<br>Val        | cgg<br>Arg        | Asn               | cta<br>Leu        | ca.<br>Gln        | g                 | gcc<br>Ala        | Lys               | gct<br>Ala        | cat<br>His        | gaa<br>Glu        | ctt<br>Leu        | cca<br>Pro        |                   | agt<br>Ser        |                   | 1357 |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
|                   |                   | 415               |                   |                   |                   |                   | 420               |                   | _++               |                   | ++0               | 425               | +++               | ~~~               | act               | 1405 |
| Cys               | Leu<br>430        | aag<br>Lys        | Phe               | gac<br>Asp        | Cys               | ggt<br>Gly<br>435 | Val               | Gln               | lie               | Gln               | Leu<br>440        | gga<br>Gly        | Phe               | Ala               | Ala               | 1403 |
| gag<br>Glu<br>445 | ttt<br>Phe        | tcc<br>Ser        | aat<br>Asn        | gtc<br>Val        | atg<br>Met<br>450 | atc<br>Ile        | atc<br>Ile        | tat<br>Tyr        | aca<br>Thr        | agt<br>Ser<br>455 | ata<br>lle        | gtt<br>Val        | tac<br>Tyr        | aaa<br>Lys        | cca<br>Pro<br>460 | 1453 |
| ccg<br>Pro        | gag<br>Glu        | ata<br>Ile        | ata<br>He         | atg<br>Met<br>465 | tgt<br>Cys        | gat<br>Asp        | gcc<br>Ala        | tac<br>Tyr        | gtt<br>Val<br>470 | act<br>Thr        | gat<br>Asp        | ttt<br>Phe        | cca<br>Pro        | ctt<br>Leu<br>475 | gat<br>Asp        | 1501 |
| cta<br>Leu        | gat<br>Asp        | att<br>lle        | gat<br>Asp<br>480 | cca<br>Pro        | aaa<br>Lys        | gat<br>Asp        | gca<br>Ala        | aat<br>Asn<br>485 | aaa<br>Lys        | ggc<br>Gly        | aca<br>Thr        | cct<br>Pro        | gaa<br>Glu<br>490 | gaa<br>Glu        | act<br>Thr        | 1549 |
| ggc<br>Gly        | agc<br>Ser        | tac<br>Tyr<br>495 | ttg<br>Leu        | gta<br>Val        | tca<br>Ser        | aag<br>Lys        | gat<br>Asp<br>500 | ctt<br>Leu        | ccc<br>Pro        | aag<br>Lys        | cat<br>His        | tgc<br>Cys<br>505 | ctc<br>Leu        | tat<br>Tyr        | acc<br>Thr        | 1597 |
| aga<br>Arg        | ctc<br>Leu<br>510 | agt<br>Ser        | tca<br>Ser        | ctg<br>Leu        | caa<br>G n        | aaa<br>Lys<br>515 | tta<br>Leu        | aag<br>Lys        | gaa<br>Glu        | cat<br>His        | cta<br>Leu<br>520 | gtc<br>Val        | ttc<br>Phe        | aca<br>Thr        | gta<br>Val        | 1645 |
| tgt<br>Cys<br>525 | tta<br>Leu        | tca<br>Ser        | tat<br>Tyr        | cag<br>Gln        | tac<br>Tyr<br>530 | tca<br>Ser        | gga<br>Gly        | ttg<br>Leu        | gaa<br>Glu        | gat<br>Asp<br>535 | act<br>Thr        | gta<br>Val        | gag<br>Glu        | gac<br>Asp        | aag<br>Lys<br>540 | 1693 |
| cag<br>Gln        | gaa<br>Glu        | gtg<br>Val        | aat<br>Asn        | gtt<br>Val<br>545 | ggg<br>Gly        | aaa<br>Lys        | cct<br>Pro        | ctc<br>Leu        | att<br>  e<br>550 | gct<br>Ala        | aaa<br>Lys        | tta<br>Leu        | gac<br>Asp        | atg<br>Met<br>555 | cat<br>His        | 1741 |
| cga<br>Arg        | ggt<br>Gly        | Leu               | gga<br>Gly<br>560 | Arg               | Lys               | Thr               | Cys               | Phe               | Gln               | Thr               | Cys               | ctt<br>Leu        | Met               | Ser               | aat<br>Asn        | 1789 |
| ggt<br>Gly        | cct<br>Pro        | tac<br>Tyr<br>575 | cag<br>Gln        | agt<br>Ser        | tct<br>Ser        | gca<br>Ala        | gcc<br>Ala<br>580 | acc<br>Thr        | tca<br>Ser        | gga<br>Gly        | gga<br>Gly        | gca<br>Ala<br>585 | ggg<br>Gly        | cat<br>His        | tat<br>Tyr        | 1837 |
| cac<br>His        | tca<br>Ser<br>590 | ttg<br>Leu        | caa<br>G n        | gac<br>Asp        | cca<br>Pro        | ttc<br>Phe<br>595 | cat<br>His        | ggt<br>Gly        | gtt<br>Val        | tac<br>Tyr        | cat<br>His<br>600 | tca<br>Ser        | cat<br>His        | cct<br>Pro        | ggt<br>Gly        | 1885 |
| aat<br>Asn<br>605 | cca<br>Pro        | agt<br>Ser        | aat<br>Asn        | gtt<br>Val        | aca<br>Thr<br>610 | cca<br>Pro        | gca<br>Ala        | gat<br>Asp        | agc<br>Ser        | tgt<br>Cys<br>615 | cat<br>His        | tgc<br>Cys        | agc<br>Ser        | cgg<br>Arg        | act<br>Thr<br>620 | 1933 |
| cca<br>Pro        | gat<br>Asp        | gca<br>Ala        | ttt<br>Phe        | att<br>lle<br>625 | tca<br>Ser        | agt<br>Ser        | ttc<br>Phe        | gct<br>Ala        | cac<br>His<br>630 | cat<br>His        | gct<br>Ala        | tca<br>Ser        | tgt<br>Cys        | cat<br>His<br>635 | ttt<br>Phe        | 1981 |
| agt<br>Ser        | aga<br>Arg        | agt<br>Ser        | aat<br>Asn        | gtg<br>Val        | cca<br>Pro        | gta<br>Val        | gag<br>Glu        | aca<br>Thr        | act<br>Thr        | gat<br>Asp        | gaa<br>Glu        | ata<br>Ile        | cca<br>Pro        | ttt<br>Phe        | agt<br>Ser        | 2029 |



2079

gttagcataa ttttagatgc ctgtgaaata gtactgcact tacataaagt gagacattgt 2139 gaaaaggcaa atttgtatat gtagagaaag aatagtagta actgttcat agcaaacttc 2199

aggactttga gatgttgaaa ttacattatt taattacaga cttcctcttt ct 2251

<210> 131

<211> 824

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<213> Homo sapiens

<400> 131

Met Ser Leu Leu Gly Asp Pro Leu Gln Ala Leu Pro Pro Ser Ala Ala 1 5 10 15

Pro Thr Gly Pro Leu Leu Ala Pro Pro Ala Gly Ala Thr Leu Asn Arg 20 25 30

Leu Arg Glu Pro Leu Leu Arg Arg Leu Ser Glu Leu Leu Asp Gln Ala 35 40 45

Pro Glu Gly Arg Gly Trp Arg Arg Leu Ala Glu Leu Ala Gly Ser Arg 50 55 60

Gly Arg Leu Arg Leu Ser Cys Leu Asp Leu Glu Gln Cys Ser Leu Lys 65 70 75 80

Val Leu Glu Pro Glu Gly Ser Pro Ser Leu Cys Leu Leu Lys Leu Met

Gly Glu Lys Gly Cys Thr Val Thr Glu Leu Ser Asp Phe Leu Gln Ala 100 105 110

Met Glu His Thr Glu Val Leu Gln Leu Leu Ser Pro Pro Gly Ile Lys 115 120 125

lle Thr Val Asn Pro Glu Ser Lys Ala Val Leu Ala Gly Gln Phe Val 130 135 140

Lys Leu Cys Cys Arg Ala Thr Gly His Pro Phe Val Gln Tyr Gln Trp 145 150 155 160

Phe Lys Met Asn Lys Glu lle Pro Asn Gly Asn Thr Ser Glu Leu lle 165 170 175

Phe Asn Ala Val His Val Lys Asp Ala Gly Phe Tyr Val Cys Arg Val 180 185 190

Asn Asn Phe Thr Phe Glu Phe Ser Gln Trp Ser Gln Leu Asp Val 195 200 205

| Cys        | Asp<br>210 |            | Pro        | GI          | er         | Phe<br>215 |             | Arg        | Ser        | Val        | Asp<br>220 |            |            | Ser        | Glu        |
|------------|------------|------------|------------|-------------|------------|------------|-------------|------------|------------|------------|------------|------------|------------|------------|------------|
| Ser<br>225 |            | Leu        | ı Gin      | lle         | Cys<br>230 |            | Glu         | Pro        | Thr        | Ser<br>235 |            | Lys        | Leu        | Met        | Pro<br>240 |
| Gly        | Ser        | Thr        | Leu        | Va I<br>245 |            | Gln        | Cys         | Val        | Ala<br>250 |            | Gly        | Ser        | Pro        | lle<br>255 |            |
| His        | Tyr        | Gln        | Trp<br>260 |             | Lys        | Asn        | Glu         | Leu<br>265 |            | Leu        | Thr        | His        | Glu<br>270 |            | Lys        |
| Lys        | Leu        | Tyr<br>275 | Met        | Val         | Pro        | Tyr        | Va l<br>280 |            | Leu        | Glu        | His        | Gln<br>285 | -          | Thr        | Tyr        |
| Trp        | Cys<br>290 |            | Val        | Tyr         | Asn        | Asp<br>295 |             | Asp        | Ser        | Gln        | Asp<br>300 |            | Lys        | Lys        | Val        |
| Glu<br>305 | He         | He         | lle        | Gly         | Arg<br>310 | Thr        | Asp         | Glu        | Ala        | Val<br>315 |            | Cys        | Thr        | Glu        | Asp<br>320 |
| Glu        | Leu        | Asn        | Asn        | Leu<br>325  | Gly        | His        | Pro         | Asp        | Asn<br>330 | Lys        | Glu        | Gln        | Thr        | Thr<br>335 | Asp        |
| Gln        | Pro        | Leu        | Ala<br>340 | Lys         | Asp        | Lys        | Val         | Ala<br>345 | Leu        | Leu        | lle        | Gly        | Asn<br>350 | Met        | Asn        |
| Tyr        | Arg        | Glu<br>355 | His        | Pro         | Lys        | Leu        | Lys<br>360  | Ala        | Pro        | Leu        | Val        | Asp<br>365 | Val        | Tyr        | Glu        |
| Leu        | Thr<br>370 | Asn        | Leu        | Leu         | Arg        | Gln<br>375 | Leu         | Asp        | Phe        | Lys        | Val<br>380 | Val        | Ser        | Leu        | Leu        |
| Asp<br>385 | Leu        | Thr        | Glu        | Tyr         | G1u<br>390 | Met        | Arg         | Asn        | Ala        | Val<br>395 | Asp        | Glu        | Phe        | Leu        | Leu<br>400 |
| Leu        | Leu        | Asp        | Lys        | Gly<br>405  | Val        | Tyr        | Gly         | Leu        | Leu<br>410 | Tyr        | Tyr        | Ala        | Gly        | His<br>415 | Gly        |
| Tyr        | Glu        | Asn        | Phe<br>420 | Gly         | Asn        | Ser        | Phe         | Met<br>425 | Val        | Pro        | Val        | Asp        | Ala<br>430 | Pro        | Asn        |
| Pro        | Tyr        | Arg<br>435 | Ser        | Glu         | Asn        | Cys        | Leu<br>440  | Cys        | Val        | Gln        | Asn        | 11e<br>445 | Leu        | Lys        | Leu        |
| Met        | GIn<br>450 | Glu        | Lys        | Glu         | Thr        | Gly<br>455 | Leu         | Asn        | Val        | Phe        | Leu<br>460 | Leu        | Asp        | Met        | Cys        |
| Arg<br>465 | Lys        | Arg        | Asn        | Asp         | Tyr<br>470 | Asp        | Asp         | Thr        | lle        | Pro<br>475 | He         | Leu        | Asp        | Ala        | Leu<br>480 |
| Lys        | Val        | Thr        | Ala        | Asn<br>485  | lle        | Val        | Phe         | Gly        | Tyr<br>490 | Ala        | Thr        | Cys        | Gln        | Gly<br>495 | Ala        |
| Glu        | Ala        | Phe        | Glu<br>500 | lle         | Gln        | His        | Ser         | Gly<br>505 | Leu        | A∣a        | Asn        | Gly        | 11e<br>510 | Phe        | Met        |
| Lys        | Phe        | Leu        | Lys        | Asp         | Arg        | Leu        | Leu         | Glu        | Asp        | Lys        | Lys        | He         | Thr        | Val        | Leu        |



Leu Asp Glu Val Ala Glu Asp Met Gly Lys Cys His Leu Thr Lys Gly 530 535 540

Lys Gln Ala Leu Glu Ile Arg Ser Ser Leu Ser Glu Lys Arg Ala Leu 545 550 555 560

Thr Asp Pro 11e Gln Gly Thr Glu Tyr Ser Ala Glu Ser Leu Val Arg 565 570 575

Asn Leu Gln Trp Ala Lys Ala His Glu Leu Pro Glu Ser Met Cys Leu 580 585 590

Lys Phe Asp Cys Gly Val Gln Ile Gln Leu Gly Phe Ala Ala Glu Phe 595 600 605

Ser Asn Val Met IIe IIe Tyr Thr Ser IIe Val Tyr Lys Pro Pro Glu 610 620

lle lle Met Cys Asp Ala Tyr Val Thr Asp Phe Pro Leu Asp Leu Asp 625 630 635 640

lle Asp Pro Lys Asp Ala Asn Lys Gly Thr Pro Glu Glu Thr Gly Ser 645 650 655

Tyr Leu Val Ser Lys Asp Leu Pro Lys His Cys Leu Tyr Thr Arg Leu 660 665 670

Ser Ser Leu Gln Lys Leu Lys Glu His Leu Val Phe Thr Val Cys Leu 675 680 685

Ser Tyr Gln Tyr Ser Gly Leu Glu Asp Thr Val Glu Asp Lys Gln Glu 690 695 700

Val Asn Val Gly Lys Pro Leu IIe Ala Lys Leu Asp Met His Arg Gly 705 710 715 720

Leu Gly Arg Lys Thr Cys Phe Gln Thr Cys Leu Met Ser Asn Gly Pro 725 730 735

Tyr Gln Ser Ser Ala Ala Thr Ser Gly Gly Ala Gly His Tyr His Ser 740 745 750

Leu Gln Asp Pro Phe His Gly Val Tyr His Ser His Pro Gly Asn Pro 755 760 765

Ser Asn Val Thr Pro Ala Asp Ser Cys His Cys Ser Arg Thr Pro Asp 770 780

Ala Phe IIe Ser Ser Phe Ala His His Ala Ser Cys His Phe Ser Arg 785 790 795 800

Ser Asn Val Pro Val Glu Thr Thr Asp Glu lle Pro Phe Ser Phe Ser 805 810 815

Asp Arg Leu Arg lle Ser Glu Lys 820

| <21<br><21       | <pre>(210&gt; 132 (211&gt; 2828 (212&gt; DNA (213&gt; Homo sapiens</pre>           |                   |                   |                   |                  |                  |                   |                   |                   |                  |                  |                   |                   |                   |                   |     |
|------------------|--|-------------------|-------------------|-------------------|------------------|------------------|-------------------|-------------------|-------------------|------------------|------------------|-------------------|-------------------|-------------------|-------------------|-----|
| <22              | <220><br><221> CDS<br><222> (165) (2636)   |                   |                   |                   |                  |                  |                   |                   |                   |                  |                  |                   |                   |                   |                   |     |
|                  | <400> 132<br>ggggcgggga gcggacttcc tcctctgagg gccgtgccgc gctgccagat ttgttcttcc     |                   |                   |                   |                  |                  |                   |                   |                   |                  |                  |                   |                   |                   |                   | 60  |
| gcc              | gcccctgcct ccgcggctcg gaggcgagcg gaaggtgccc cggggccgag gcccgtgacg                  |                   |                   |                   |                  |                  |                   |                   |                   |                  |                  |                   |                   |                   |                   | 120 |
| ggg              | gggcgggcgg gagccccggc agtccggggt cgccggcgag ggcc atg tcg ctg ttg Met Ser Leu Leu 1 |                   |                   |                   |                  |                  |                   |                   |                   |                  |                  |                   |                   |                   |                   | 176 |
| ggg<br>Gly<br>5  | Asp  | ccg<br>Pro        | cta<br>Leu        | cag<br>Gln        | gcc<br>Ala<br>10 | Leu              | ccg<br>Pro        | ccc<br>Pro        | tcg<br>Ser        | gcc<br>Ala<br>15 | Ala              | ccc<br>Pro        | acg<br>Thr        | ggg<br>Gly        | ccg<br>Pro<br>20  | 224 |
| ctg<br>Leu       | ctc<br>Leu   | gcc<br>Ala        | cct<br>Pro        | ccg<br>Pro<br>25  | gcc<br>Ala       | ggc<br>Gly       | gcg<br>Ala        | acc<br>Thr        | ctc<br>Leu<br>30  | aac<br>Asn       | cgc<br>Arg       | ctg<br>Leu        | cgg<br>Arg        | gag<br>Glu<br>35  | ccg<br>Pro        | 272 |
| ctg<br>Leu       | ctg<br>Leu   | cgg<br>Arg        | agg<br>Arg<br>40  | ctc<br>Leu        | agc<br>Ser       | gag<br>G u       | ctc<br>Leu        | ctg<br>Leu<br>45  | gat<br>Asp        | cag<br>Gln       | gcg<br>Ala       | ccc<br>Pro        | gag<br>Glu<br>50  | ggc<br>Gly        | cgg<br>Arg        | 320 |
| ggc<br>Gly       | tgg<br>Trp   | agg<br>Arg<br>55  | aga<br>Arg        | ctg<br>Leu        | gcg<br>Ala       | gag<br>Glu       | ctg<br>Leu<br>60  | gcg<br>Ala        | ggg<br>Gly        | agt<br>Ser       | cgc<br>Arg       | ggg<br>Gly<br>65  | cgc<br>Arg        | ctc<br>Leu        | cgc<br>Arg        | 368 |
| ctc<br>Leu       | agt<br>Ser<br>70   | tgc<br>Cys        | cta<br>Leu        | gac<br>Asp        | ctg<br>Leu       | gag<br>Glu<br>75 | cag<br>Gln        | tgt<br>Cys        | tct<br>Ser        | ctt<br>Leu       | aag<br>Lys<br>80 | gta<br>Val        | ctg<br>Leu        | gag<br>Glu        | cct<br>Pro        | 416 |
| gaa<br>Glu<br>85 | gga<br>Gly   | agc<br>Ser        | ccc<br>Pro        | agc<br>Ser        | ctg<br>Leu<br>90 | tgt<br>Cys       | ctg<br>Leu        | ctg<br>Leu        | aag<br>Lys        | tta<br>Leu<br>95 | atg<br>Met       | ggt<br>Gly        | gaa<br>Glu        | aaa<br>Lys        | ggt<br>Gly<br>100 | 464 |
| tgc<br>Cys       | aca<br>Thr   | gtc<br>Val        | aca<br>Thr        | gaa<br>Glu<br>105 | ttg<br>Leu       | agt<br>Ser       | gat<br>Asp        | ttc<br>Phe        | ctg<br>Leu<br>110 | cag<br>Gln       | gct<br>Ala       | atg<br>Met        | gaa<br>Glu        | cac<br>His<br>115 | act<br>Thr        | 512 |
| gaa<br>Glu       | gtt<br>Val   | ctt<br>Leu        | cag<br>Gln<br>120 | ctt<br>Leu        | ctc<br>Leu       | agc<br>Ser       | ccc<br>Pro        | cca<br>Pro<br>125 | gga<br>Gly        | ata<br>He        | aag<br>Lys       | att<br>Ile        | act<br>Thr<br>130 | gta<br>Val        | aac<br>Asn        | 560 |
| cca<br>Pro       | gag<br>Glu   | tca<br>Ser<br>135 | aag<br>Lys        | gca<br>Ala        | gtc<br>Val       | ttg<br>Leu       | gct<br>Ala<br>140 | gga<br>Gly        | cag<br>Gln        | ttt<br>Phe       | gtg<br>Val       | aaa<br>Lys<br>145 | ctg<br>Leu        | tgt<br>Cys        | tgc<br>Cys        | 608 |
| cgg<br>Arg       | gca<br>Ala   | act<br>Thr        | gga<br>Gly        | cat<br>His        | cct<br>Pro       | ttt<br>Phe       | gtt<br>Val        | caa<br>Gln        | tat<br>Tyr        | cag<br>Gln       | tgg<br>Trp       | ttc<br>Phe        | aaa<br>Lys        | atg<br>Met        | aat<br>Asn        | 656 |

|           |                   | att<br>lle        |            |            |            |                   |            |            |            |            |                   |            |            |            |            | 704  |
|-----------|-------------------|-------------------|------------|------------|------------|-------------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|------|
|           |                   | aaa<br>Lys        |            |            |            |                   |            |            |            |            |                   |            |            |            |            | 752  |
|           |                   | gaa<br>Glu        |            |            |            |                   |            |            |            |            |                   |            |            |            |            | 800  |
|           |                   | ttc<br>Phe<br>215 |            |            |            |                   |            |            |            |            |                   |            |            |            |            | 848  |
| atc<br>He | tgt<br>Cys<br>230 | gtt<br>Val        | gaa<br>Glu | cca<br>Pro | act<br>Thr | tcc<br>Ser<br>235 | caa<br>Gln | aag<br>Lys | ctg<br>Leu | atg<br>Met | cca<br>Pro<br>240 | ggc<br>Gly | agc<br>Ser | aca<br>Thr | ttg<br>Leu | 896  |
|           |                   | cag<br>Gln        |            |            |            |                   |            |            |            |            |                   |            |            |            |            | 944  |
|           |                   | aat<br>Asn        |            |            |            |                   |            |            |            |            |                   |            |            |            |            | 992  |
|           |                   | tat<br>Tyr        |            |            |            |                   |            |            |            |            |                   |            |            |            |            | 1040 |
|           |                   | gat<br>Asp<br>295 |            |            |            |                   |            |            |            |            |                   |            |            |            |            | 1088 |
|           |                   | aca<br>Thr        |            |            |            |                   |            |            |            |            |                   |            |            |            |            | 1136 |
|           |                   | cat<br>His        |            |            |            |                   |            |            |            |            |                   |            |            |            |            | 1184 |
| -         | -                 | aag<br>Lys        | _          | _          |            |                   |            |            |            | _          |                   |            |            |            |            | 1232 |
|           |                   | ctc<br>Leu        |            |            |            |                   | Val        |            |            |            |                   |            |            |            |            | 1280 |
|           | Arg               | cag<br>Gln<br>375 |            |            |            |                   |            |            |            |            |                   |            |            |            |            | 1328 |

| ta<br>Ty          | it ga<br>r Gl<br>39 | u iyie            | tg ca<br>et A      | gt aa<br>rg As        | sn Al                      | t gt<br>a Va<br>39    | g ga<br>il As<br>95       | t ga;<br>p Gli        | g tt<br>u Ph       | t tt<br>e Le       | a ct<br>u Le<br>40    | u Le                  | t<br>u Le           | ga<br>u As         | ac aag<br>sp Lys       | 1376 |
|-------------------|---------------------|-------------------|--------------------|-----------------------|----------------------------|-----------------------|---------------------------|-----------------------|--------------------|--------------------|-----------------------|-----------------------|---------------------|--------------------|------------------------|------|
| gg<br>Gl<br>40    | y va                | a ta<br>I Ty      | at gg<br>/r G      | gg tt<br>ly Le        | a tt<br>eu Le<br>41        | u Iy                  | r Ty                      | t gca<br>r Ala        | agg<br>aGI         | а са<br>у Ні<br>41 | s Gl                  | t ta<br>y Ty          | t ga<br>r Gl        | a aa<br>u As       | nt ttt<br>n Phe<br>420 | 1424 |
| gg<br>Gl          | g aa<br>y As        | c ag<br>n Se      | go tt<br>er Ph     | c at<br>ne Me<br>42   | et Va                      | c cc<br>I Pr          | c gt <sup>.</sup><br>o Va | t gat<br>I Asp        | gc<br>6 Ala<br>430 | a Pr               | a aa<br>o As          | t cc<br>n Pr          | a ta<br>o Ty        | t ag<br>r Ar<br>43 | g tct<br>g Ser<br>5    | 1472 |
| ga<br>Gl          | a aa<br>u Asi       | t tg<br>n Cy      | t ct<br>s Le<br>44 | eu Cy                 | t gt<br>s Va               | a ca<br>I Gl          | a aat<br>n Asr            | t ata<br>n Ile<br>445 | e Lei              | g aa<br>u Ly       | a tt;<br>s Lei        | g at;<br>u Me         | g ca<br>t G1<br>450 | n Gi               | a aaa<br>u Lys         | 1520 |
| gaa<br>Glu        | a act<br>u Thi      | t gg<br>Gl<br>45  | y Le               | t aa<br>u As          | t gt,<br>n Va              | g tte                 | c tta<br>e Leu<br>460     | ı Leu                 | gat<br>Asp         | t ata              | g tgt<br>t Cys        | t agg<br>s Arg<br>465 | g Lys               | a aga<br>s Ar      | a aat<br>g Asn         | 1568 |
| gac<br>Asp        | tac<br>Tyr<br>470   | ' As              | t ga<br>p As       | t ac<br>p Th          | c at <sup>.</sup><br>r Ile | t cca<br>e Pro<br>475 | o lle                     | ttg<br>Leu            | gat<br>Asp         | gca<br>Ala         | a cta<br>a Lei<br>480 | ı Lys                 | a gto<br>s Val      | aco<br>Thi         | c gcc<br>r Ala         | 1616 |
| aat<br>Asr<br>485 | ı IIE               | gt,<br>Va         | g tt<br>I Ph       | t gga<br>e Gly        | a tat<br>y Tyr<br>490      | - Ala                 | acg<br>Thr                | tgt<br>Cys            | caa<br>Gln         | gga<br>Gly<br>495  | / Ala                 | gaa<br>Glu            | gct<br>Ala          | ttt<br>Phe         | gaa<br>Glu<br>500      | 1664 |
| ato<br>Ile        | cag<br>Gln          | ca<br>His         | t tc<br>s Se       | t gga<br>r Gly<br>505 | / Lei                      | g gca<br>ı Ala        | a aat<br>a Asn            | gga<br>Gly            | atc<br>lle<br>510  | Phe                | atg<br>Met            | aaa<br>Lys            | ttt<br>Phe          | tta<br>Leu<br>515  | aaa<br>Lys             | 1712 |
| gac<br>Asp        | aga<br>Arg          | tta<br>Leu        | tta<br>Lei<br>520  | ı Glu                 | ı gat<br>ı Asp             | aag<br>Lys            | aaa<br>Lys                | atc<br>Ile<br>525     | act<br>Thr         | gtg<br>Val         | tta<br>Leu            | ctg<br>Leu            | gat<br>Asp<br>530   | gaa<br>Glu         | gtt<br>Val             | 1760 |
| gca<br>Ala        | gaa<br>Glu          | gat<br>Asp<br>535 | Met                | : Gly                 | Lys                        | Cvs                   | cac<br>His<br>540         | Leu                   | acc<br>Thr         | aaa<br>Lys         | ggc<br>Gly            | aaa<br>Lys<br>545     | cag<br>G n          | gct<br>Ala         | cta<br>Leu             | 1808 |
| gag<br>Glu        | att<br>lle<br>550   | cga<br>Arg        | agt<br>Ser         | agt<br>Ser            | tta<br>Leu                 | tct<br>Ser<br>555     | gag<br>Glu                | aag<br>Lys            | aga<br>Arg         | gca<br>Ala         | ctt<br>Leu<br>560     | act<br>Thr            | gat<br>Asp          | cca<br>Pro         | ata<br>He              | 1856 |
| cag<br>Gln<br>565 | gga<br>Gly          | aca<br>Thr        | gaa<br>Glu         | tat<br>Tyr            | tct<br>Ser<br>570          | gct<br>Ala            | gaa<br>Glu                | tct<br>Ser            | ctt<br>Leu         | gtg<br>Val<br>575  | cgg<br>Arg            | aat<br>Asn            | cta<br>Leu          | cag<br>Gin         | tgg<br>Trp<br>580      | 1904 |
| gcc<br>Ala        | aag<br>Lys          | gct<br>Ala        | cat<br>His         | gaa<br>Glu<br>585     | ctt<br>Leu                 | cca<br>Pro            | gaa<br>Glu                | Ser                   | atg<br>Met<br>590  | tgt<br>Cys         | ctt<br>Leu            | aag<br>Lys            | ttt<br>Phe          | gac<br>Asp<br>595  | tgt<br>Cys             | 1952 |
| ggt<br>Gly        | gtt<br>Val          | cag<br>Gln        | att<br>lle<br>600  | caa<br>Gln            | tta<br>Leu                 | gga<br>Gly            | ttt<br>Phe                | gca<br>Ala<br>605     | gct<br>Ala         | gag<br>Glu         | ttt<br>Phe            | tcc<br>Ser            | aat<br>Asn<br>610   | gtc<br>Val         | atg<br>Met             | 2000 |
| atc<br>lle        | atc<br>lle          | tat<br>Tyr        | aca<br>Thr         | agt<br>Ser            | ata<br>Ile                 | gtt<br>Val            | tac<br>Tyr                | aaa<br>Lys I          | cca<br>Pro         | ccg<br>Pro         | gag<br>Glu            | ata<br>Ile            | ata<br>Ile          | atg<br>Met         | tgt<br>Cys             | 2048 |

| gat go<br>Asp Al<br>63    | a Tyr                 | gtt<br>Val        | act<br>Thr        | gat<br>Asp        | ttt<br>Phe<br>635 | Pro               | ctt<br>Leu        | gat<br>Asp        | cta<br>Leu        | gat<br>Asp<br>640 | He                | gat<br>Asp        | cca<br>Pro        | aaa<br>Lys        | 2096 |
|---------------------------|-----------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| gat go<br>Asp Al<br>645   | a aat<br>a Asn        | aaa<br>Lys        | ggc<br>Gly        | aca<br>Thr<br>650 | cct<br>Pro        | gaa<br>G u        | gaa<br>Glu        | act<br>Thr        | ggc<br>Gly<br>655 | agc<br>Ser        | tac<br>Tyr        | ttg<br>Leu        | gta<br>Val        | tca<br>Ser<br>660 | 2144 |
| aag ga<br>Lys As          | t ctt<br>p Leu        | ccc<br>Pro        | aag<br>Lys<br>665 | cat<br>His        | tgc<br>Cys        | ctc<br>Leu        | tat<br>Tyr        | acc<br>Thr<br>670 | Arg               | ctc<br>Leu        | agt<br>Ser        | tca<br>Ser        | ctg<br>Leu<br>675 | Gln               | 2192 |
| aaa tt<br>Lys Le          | a aag<br>u Lys        | gaa<br>Glu<br>680 | cat<br>His        | cta<br>Leu        | gtc<br>Val        | ttc<br>Phe        | aca<br>Thr<br>685 | gta<br>Val        | tgt<br>Cys        | tta<br>Leu        | tca<br>Ser        | tat<br>Tyr<br>690 | cag<br>G n        | tac<br>Tyr        | 2240 |
| tca gg<br>Ser Gl          | a ttg<br>y Leu<br>695 | gaa<br>Glu        | gat<br>Asp        | act<br>Thr        | gta<br>Val        | gag<br>Glu<br>700 | gac<br>Asp        | aag<br>Lys        | cag<br>G n        | gaa<br>Glu        | gtg<br>Val<br>705 | aat<br>Asn        | gtt<br>Val        | ggg<br>Gly        | 2288 |
| aaa cc<br>Lys Pro<br>710  | Leu                   | att<br>lle        | gct<br>Ala        | aaa<br>Lys        | tta<br>Leu<br>715 | gac<br>Asp        | atg<br>Met        | cat<br>His        | cga<br>Arg        | ggt<br>Gly<br>720 | ttg<br>Leu        | gga<br>Gly        | agg<br>Arg        | aag<br>Lys        | 2336 |
| act tgo<br>Thr Cys<br>725 | ttt<br>Phe            | caa<br>GIn        | act<br>Thr        | tgt<br>Cys<br>730 | ctt<br>Leu        | atg<br>Met        | tct<br>Ser        | aat<br>Asn        | ggt<br>Gly<br>735 | cct<br>Pro        | tac<br>Tyr        | cag<br>G n        | agt<br>Ser        | tct<br>Ser<br>740 | 2384 |
| gca gco<br>Ala Ala        | acc<br>Thr            | tca<br>Ser        | gga<br>Gly<br>745 | gga<br>Gly        | gca<br>Ala        | ggg<br>Gly        | cat<br>His        | tat<br>Tyr<br>750 | cac<br>His        | tca<br>Ser        | ttg<br>Leu        | caa<br>Gln        | gac<br>Asp<br>755 | cca<br>Pro        | 2432 |
| ttc cat<br>Phe His        | ggt                   | gtt<br>Val<br>760 | tac<br>Tyr        | cat<br>His        | tca<br>Ser        | cat<br>His        | cct<br>Pro<br>765 | ggt<br>Gly        | aat<br>Asn        | cca<br>Pro        | agt<br>Ser        | aat<br>Asn<br>770 | gtt<br>Val        | aca<br>Thr        | 2480 |
| cca gca<br>Pro Ala        | gat<br>Asp<br>775     | agc<br>Ser        | tgt<br>Cys        | cat<br>His        | tgc<br>Cys        | agc<br>Ser<br>780 | cgg<br>Arg        | act<br>Thr        | cca<br>Pro        | gat<br>Asp        | gca<br>Ala<br>785 | ttt<br>Phe        | att<br>He         | tca<br>Ser        | 2528 |
| agt tto<br>Ser Phe<br>790 | Ala                   | cac<br>His        | cat<br>His        | Ala               | tca<br>Ser<br>795 | tgt<br>Cys        | cat<br>His        | ttt<br>Phe        | Ser               | aga<br>Arg<br>800 | agt<br>Ser        | aat<br>Asn        | gtg<br>Val        | cca<br>Pro        | 2576 |
| gta gag<br>Val Glu<br>805 | aca<br>Thr            | act<br>Thr        | Asp               | gaa<br>Glu<br>810 | ata<br>He         | cca<br>Pro        | ttt<br>Phe        | Ser               | ttc<br>Phe<br>815 | tct<br>Ser        | gac<br>Asp        | agg<br>Arg        | Leu               | aga<br>Arg<br>820 | 2624 |
| att tct<br>lle Ser        | gaa<br>Glu            | aaa<br>Lys        | tgac              | ctcc <sup>.</sup> | tt g              | tttt              | tgaa              | a gt              | tagc              | ataa              | ttt               | taga              | tgc               |                   | 2676 |
| ctgtgaa                   | ata g                 | tact              | gcac              | t tad             | cata              | aagt              | gag               | acat              | tgt į             | gaaa              | aggc              | aa a              | tttg              | tatat             | 2736 |
| gtagaga                   | aag a                 | atag <sup>.</sup> | tagt              | a act             | tgtt              | tcat              | agc               | aaac              | ttc               | agga              | cttt              | ga g              | atgt              | tgaaa             | 2796 |
| ttacatt                   | att t                 | aatta             | acag              | a ct              | tcct              | cttt              | ct                |                   |                   |                   |                   |                   |                   |                   | 2828 |

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Glu Val Ala Ser IIe Leu Gln Ala Asp Leu Gln Asn Gly Leu Asn Lys 35 40 45

Cys Glu Val Ser His Arg Arg Ala Phe His Gly Trp Asn Glu Phe Asp 50 55 60

lle Ser Glu Asp Glu Pro Leu Trp Lys Lys Tyr lle Ser Gln Phe Lys
65 70 75 80

Asn Pro Leu Ile Met Leu Leu Leu Ala Ser Ala Val Ile Ser Val Leu 85 90 95

Met His Gln Phe Asp Asp Ala Val Ser lle Thr Val Ala lle Leu lle 100 105 110

Val Val Thr Val Ala Phe Val Gin Glu Tyr Arg Ser Glu Lys Ser Leu 115 120 125

Glu Glu Leu Ser Lys Leu Val Pro Pro Glu Cys His Cys Val Arg Glu 130 135 140

Gly Lys Leu Glu His Thr Leu Ala Arg Asp Leu Val Pro Gly Asp Thr 145 150 155 160

Val Cys Leu Ser Val Gly Asp Arg Val Pro Ala Asp Leu Arg Leu Phe 165 170 175

Glu Ala Val Asp Leu Ser lle Asp Glu Ser Ser Leu Thr Gly Glu Thr 180 185 190

Thr Pro Cys Ser Lys Val Thr Ala Pro Gin Pro Ala Ala Thr Asn Gly 195 200 205

Asp Leu Ala Ser Arg Ser Asn IIe Ala Phe Met Gly Thr Leu Val Arg 210 215 220

Cys Gly Lys Ala Lys Gly Val Val IIe Gly Thr Gly Glu Asn Ser Glu 225 230 235 240

Phe Gly Glu Val Phe Lys Met Met Gln Ala Glu Glu Ala Pro Lys Thr 245 250 255

Pro Leu Gln Lys Ser Met Asp Leu Leu Gly Lys Gln Leu Ser Phe Tyr 260 265 270

| Ser        | Phe        | Gly<br>275 | lle        | He          | Gly        | He          | lle<br>280 | Met        | Leu        | Val        | Gly        | Trp<br>285 | Leu        | Leu         | Gly        |
|------------|------------|------------|------------|-------------|------------|-------------|------------|------------|------------|------------|------------|------------|------------|-------------|------------|
| Lys        | Asp<br>290 | He         | Leu        | Glu         | Met        | Phe<br>295  | Thr        | He         | Ser        | Val        | Ser<br>300 | Leu        | Ala        | Val         | Ala        |
| Ala<br>305 | Пе         | Pro        | Glu        | Gly         | Leu<br>310 | Pro         | Пе         | Val        | Val        | Thr<br>315 | Val        | Thr        | Leu        | Ala         | Leu<br>320 |
| Gly        | Val        | Met        | Arg        | Met<br>325  | Val        | Lys         | Lys        | Arg        | Ala<br>330 | Пe         | Val        | Lys        | Lys        | Leu<br>335  | Pro        |
| lle        | Val        | Glu        | Thr<br>340 | Leu         | Gly        | Cys         | Cys        | Asn<br>345 | Val        | lle        | Cys        | Ser        | Asp<br>350 | Lys         | Thr        |
| Gly        | Thr        | Leu<br>355 | Thr        | Lys         | Asn        | Glu         | Met<br>360 | Thr        | Val        | Thr        | His        | lle<br>365 | Phe        | Thr         | Ser        |
| Asp        | Gly<br>370 | Leu        | His        | Ala         | Glu        | Va I<br>375 | Thr        | Gly        | Val        | Gly        | Tyr<br>380 | Asn        | Gln        | Phe         | Gly        |
| Glu<br>385 | Val        | He         | Val        | Asp         | Gly<br>390 | Asp         | Val        | Val        | His        | Gly<br>395 | Phe        | Tyr        | Asn        | Pro         | Ala<br>400 |
| Val        | Ser        | Arg        | He         | Va l<br>405 | Glu        | Ala         | Gly        | Cys        | Val<br>410 | Cys        | Asn        | Asp        | Ala        | Va l<br>415 | lle        |
| Arg        | Asn        | Asn        | Thr<br>420 | Leu         | Met        | Gly         | Lys        | Pro<br>425 | Thr        | Glu        | Gly        | Ala        | Leu<br>430 | lle         | Ala        |
| Leu        | Ala        | Met<br>435 | Lys        | Met         | Gly        | Leu         | Asp<br>440 | Gly        | Leu        | Gln        | Gln        | Asp<br>445 | Tyr        | lle         | Arg        |
| Lys        | Ala<br>450 | Glu        | Tyr        | Pro         | Phe        | Ser<br>455  | Ser        | Glu        | Gln        | Lys        | Trp<br>460 | Met        | Ala        | Val         | Lys        |
| Cys<br>465 | Val        | His        | Arg        | Thr         | GIn<br>470 | Gln         | Asp        | Arg        | Pro        | G1u<br>475 | lle        | Cys        | Phe        | Met         | Lys<br>480 |
| Gly        | Ala        | Tyr        | Glu        | G1n<br>485  | Val        | lle         | Lys        | Tyr        | Cys<br>490 | Thr        | Thr        | Tyr        | Gln        | Ser<br>495  | Lys        |
| Gly        | Gln        | Thr        | Leu<br>500 | Thr         | Leu        | Thr         | Gin        | G n<br>505 | Gln        | Arg        | Asp        | Val        | Tyr<br>510 | Gln         | Gln        |
| Glu        | Lys        | Ala<br>515 | Arg        | Met         | Gly        | Ser         | Ala<br>520 | Gly        | Leu        | Arg        | Val        | Leu<br>525 | Ala        | Leu         | Ala        |
| Ser        | Gly<br>530 | Pro        | Glu        | Leu         | Gly        | GIn<br>535  | Leu        | Thr        | Phe        | Leu        | Gly<br>540 | Leu        | Val        | Gly         | He         |
| 11e<br>545 | Asp        | Pro        | Pro        | Arg         | Thr<br>550 | Gly         | Val        | Lys        | Glu        | Ala<br>555 | Val        | Thr        | Thr        | Leu         | 11e<br>560 |
| Ala        | Ser        | Gly        | Val        | Ser<br>565  | lle        | Lys         | Met        | He         | Thr<br>570 | Gly        | Asp        | Ser        | Gin        | G1u<br>575  | Thr        |

| A∃a        | Val        | Ala          | 11e<br>580 | ΑI         | r          | Arg        | Leu        | Gly<br>585 |            | Tyr        | Ser        | Lys        | 550        | Ser        | Gln        |
|------------|------------|--------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| Ser        | Val        | Ser<br>595   | Gly        | Glu        | ı Glu      | He         | Asp<br>600 |            | Met        | Asp        | Val        | Gln<br>605 |            | Leu        | Ser        |
| Gln        | lle<br>610 |              | Pro        | Lys        | Val        | Ala<br>615 |            | Phe        | Tyr        | Arg        | Ala<br>620 |            | Pro        | Arg        | His        |
| Lys<br>625 |            | Lys          | lle        | He         | Lys<br>630 |            | Leu        | Gln        | Lys        | Asn<br>635 |            | Ser        | Val        | Val        | Ala<br>640 |
| Met        | Thr        | Gly          | Asp        | Gly<br>645 |            | Asn        | Asp        | Ala        | Val<br>650 |            | Leu        | Lys        | Ala        | Ala<br>655 |            |
| Пе         | Gly        | Val          | Ala<br>660 |            | Gly        | Gln        | Thr        | Gly<br>665 | Thr        | Asp        | Val        | Cys        | Lys<br>670 |            | Ala        |
| Ala        | Asp        | Met<br>675   | He         | Leu        | Val        | Asp        | Asp<br>680 | Asp        | Phe        | Gln        | Thr        | lle<br>685 |            | Ser        | Ala        |
| He         | Glu<br>690 |              | Gly        | Lys        | Gly        | lle<br>695 | Tyr        | Asn        | Asn        | He         | Lys<br>700 |            | Phe        | Val        | Arg        |
| Phe<br>705 | Gln        | Leu          | Ser        | Thr        | Ser<br>710 | He         | Ala        | Ala        | Leu        | Thr<br>715 | Leu        | He         | Ser        | Leu        | Ala<br>720 |
| Thr        | Leu        | Met          | Asn        | Phe<br>725 | Pro        | Asn        | Pro        | Leu        | Asn<br>730 | Ala        | Met        | Gln        | lle        | Leu<br>735 | Trp        |
| lle        | Asn        | lle          | 11e<br>740 | Met        | Asp        | Gly        | Pro        | Pro<br>745 | Ala        | Gln        | Ser        | Leu        | Gly<br>750 | Val        | Glu        |
| Pro        | Val        | Asp<br>755   | Lys        | Asp        | Val        | He         | Arg<br>760 | Lys        | Pro        | Pro        | Arg        | Asn<br>765 | Trp        | Lys        | Asp        |
| Ser        | 11e<br>770 | Leu          | Thr        | Lys        | Asn        | Leu<br>775 | lle        | Leu        | Lys        | He         | Leu<br>780 | Val        | Ser        | Ser        | He         |
| lle<br>785 | He         | Val          | Cys        | Gly        | Thr<br>790 | Leu        | Phe        | Val        | Phe        | Trp<br>795 | Arg        | Glu        | Leu        | Arg        | Asp<br>800 |
| Asn        | Val        | Пe           | Thr        | Pro<br>805 | Arg        | Asp        | Thr        | Thr        | Met<br>810 | Thr        | Phe        | Thr        | Cys        | Phe<br>815 | Val        |
| Phe        | Phe        | Asp          | Met<br>820 | Phe        | Asn        | Ala        | Leu        | Ser<br>825 | Ser        | Arg        | Ser        | Gln        | Thr<br>830 | Lys        | Ser        |
| Val        | Phe        | G I u<br>835 | lle        | Gly        | Leu        | Cys        | Ser<br>840 | Asn        | Arg        | Met        | Phe        | Cys<br>845 | Tyr        | Ala        | Val        |
| Leu        | Gly<br>850 | Ser          | lle        | Met        | Gly        | G n<br>855 | Leu        | Leu        | Val        | He         | Tyr<br>860 | Phe        | Pro        | Pro        | Leu        |
| GIn<br>865 | Lys        | Val          | Phe        | Gln        | Thr<br>870 | Glu        | Ser        | Leu        | Ser        | lle<br>875 | Leu        | Asp        | Leu        | Leu        | Phe<br>880 |
| Leu        | Leu        | Gly          | Leu        | Thr        | Ser        | Ser        | Val        | Cys        | He         | Val        | Ala        | Glu        | He         | lle        | Lys        |



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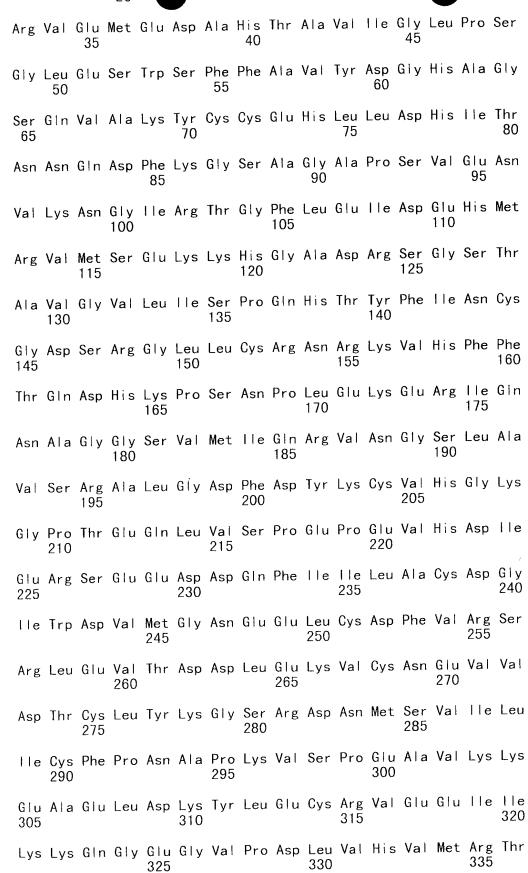
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|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| Val<br>95         | Leu               | Met               | His               | Glr               | ±<br>100          | Asp               | Asp               | Ala               | Val               | Ser<br>105        | lle               | Thr               |                   | Ala               | 11e<br>110        |      |
| ctt<br>Leu        | atc<br>Ile        | gtt<br>Val        | gtt<br>Val        | aca<br>Thr<br>115 | gtt<br>Val        | gcc<br>Ala        | ttt<br>Phe        | gtt<br>Vai        | cag<br>Gln<br>120 | gaa<br>Glu        | tat<br>Tyr        | cgt<br>Arg        | tca<br>Ser        | gaa<br>Glu<br>125 | aaa<br>Lys        | 804  |
| tct<br>Ser        | ctt<br>Leu        | gaa<br>Glu        | gaa<br>Glu<br>130 | ttg<br>Leu        | agt<br>Ser        | aaa<br>Lys        | ctt<br>Leu        | gtg<br>Val<br>135 | cca<br>Pro        | cca<br>Pro        | gaa<br>Glu        | tgc<br>Cys        | cat<br>His<br>140 | tgt<br>Cys        | gtg<br>Val        | 852  |
| cgt<br>Arg        | gaa<br>Glu        | gga<br>Gly<br>145 | aaa<br>Lys        | ttg<br>Leu        | gag<br>Glu        | cat<br>His        | aca<br>Thr<br>150 | ctt<br>Leu        | gcc<br>Ala        | cga<br>Arg        | gac<br>Asp        | ttg<br>Leu<br>155 | gtt<br>Val        | cca<br>Pro        | ggt<br>Gly        | 900  |
| gat<br>Asp        | aca<br>Thr<br>160 | gtt<br>Val        | tgc<br>Cys        | ctt<br>Leu        | tct<br>Ser        | gtt<br>Val<br>165 | ggg<br>Gly        | gat<br>Asp        | aga<br>Arg        | gtt<br>Val        | cct<br>Pro<br>170 | gct<br>Ala        | gac<br>Asp        | tta<br>Leu        | cgc<br>Arg        | 948  |
| ttg<br>Leu<br>175 | ttt<br>Phe        | gag<br>Glu        | gct<br>Ala        | gtg<br>Val        | gat<br>Asp<br>180 | ctt<br>Leu        | tcc<br>Ser        | att<br>lle        | gat<br>Asp        | gag<br>Glu<br>185 | tcc<br>Ser        | agc<br>Ser        | ttg<br>Leu        | aca<br>Thr        | ggt<br>Gly<br>190 | 996  |
| gag<br>Glu        | aca<br>Thr        | acg<br>Thr        | cct<br>Pro        | tgt<br>Cys<br>195 | tct<br>Ser        | aag<br>Lys        | gtg<br>Val        | aca<br>Thr        | gct<br>Ala<br>200 | cct<br>Pro        | cag<br>Gln        | cca<br>Pro        | gct<br>Ala        | gca<br>Ala<br>205 | act<br>Thr        | 1044 |
| aat<br>Asn        | gga<br>Gly        | gat<br>Asp        | ctt<br>Leu<br>210 | gca<br>Ala        | tcg<br>Ser        | aga<br>Arg        | agt<br>Ser        | aac<br>Asn<br>215 | att<br>  e        | gcc<br>Ala        | ttt<br>Phe        | atg<br>Met        | gga<br>Gly<br>220 | aca<br>Thr        | ctg<br>Leu        | 1092 |
| gtc<br>Val        | aga<br>Arg        | tgt<br>Cys<br>225 | ggc<br>Gly        | aaa<br>Lys        | gca<br>Ala        | aag<br>Lys        | ggt<br>Gly<br>230 | gtt<br>Val        | gtc<br>Val        | att<br>He         | gga<br>Gly        | aca<br>Thr<br>235 | gga<br>Gly        | gaa<br>Glu        | aat<br>Asn        | 1140 |
| tct<br>Ser        | gaa<br>Glu<br>240 | ttt<br>Phe        | ggg<br>Gly        | gag<br>Glu        | gtt<br>Val        | ttt<br>Phe<br>245 | aaa<br>Lys        | atg<br>Met        | atg<br>Met        | caa<br>Gln        | gca<br>Ala<br>250 | gaa<br>Glu        | gag<br>Glu        | gca<br>Ala        | cca<br>Pro        | 1188 |
| aaa<br>Lys<br>255 | acc<br>Thr        | cct<br>Pro        | ctg<br>Leu        | cag<br>Gln        | aag<br>Lys<br>260 | agc<br>Ser        | atg<br>Met        | gac<br>Asp        | ctc<br>Leu        | tta<br>Leu<br>265 | gga<br>Gly        | aaa<br>Lys        | caa<br>Gln        | ctt<br>Leu        | tcc<br>Ser<br>270 | 1236 |
| ttt<br>Phe        | tac<br>Tyr        | tcc<br>Ser        | ttt<br>Phe        | ggt<br>Gly<br>275 | ata<br>Ile        | ata<br>Ile        | gga<br>Gly        | atc<br>ile        | atc<br>lle<br>280 | atg<br>Met        | ttg<br>Leu        | gtt<br>Val        | ggc<br>Gly        | tgg<br>Trp<br>285 | tta<br>Leu        | 1284 |
| ctg<br>Leu        | gga<br>Gly        | aaa<br>Lys        | gat<br>Asp<br>290 | atc<br>Ile        | ctg<br>Leu        | gaa<br>Glu        | atg<br>Met        | ttt<br>Phe<br>295 | act<br>Thr        | att<br>Ile        | agt<br>Ser        | gta<br>Val        | agt<br>Ser<br>300 | ttg<br>Leu        | gct<br>Ala        | 1332 |
| gta<br>Val        | gca<br>Ala        | gca<br>Ala<br>305 | att<br>He         | cct<br>Pro        | gaa<br>Glu        | ggt<br>Gly        | ctc<br>Leu<br>310 | ccc<br>Pro        | att<br>He         | gtg<br>Val        | gtc<br>Val        | aca<br>Thr<br>315 | gtg<br>Val        | acg<br>Thr        | cta<br>Leu        | 1380 |
| gct<br>Ala        | ctt<br>Leu<br>320 | ggt<br>Gly        | gtt<br>Val        | atg<br>Met        | aga<br>Arg        | atg<br>Met<br>325 | gtg<br>Val        | aag<br>Lys        | aaa<br>Lys        | agg<br>Arg        | gcc<br>Ala<br>330 | att<br>lle        | gtg<br>Val        | aaa<br>Lys        | aag<br>Lys        | 1428 |

| ctg<br>Leu<br>335 | cct<br>Pro        | att<br>He         | gtt<br>Val        | gaa<br>Glu        | act<br>Thr<br>340 | ctg<br>Leu        | ggc<br>Gly        | tgc<br>Cys        | tgt<br>Cys         | aat<br>Asn<br>345 | gtg<br>Val        | att<br>He         | tgt<br>Cys        | tca<br>Ser        | gat<br>Asp<br>350 | 1476 |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|--------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| aaa<br>Lys        | act<br>Thr        | gga<br>Gly        | aca<br>Thr        | ctg<br>Leu<br>355 | acg<br>Thr        | aag<br>Lys        | aat<br>Asn        | gaa<br>Glu        | atg<br>Met<br>360  | act<br>Thr        | gtt<br>Val        | act<br>Thr        | cac<br>His        | ata<br>11e<br>365 | ttt<br>Phe        | 1524 |
| act<br>Thr        | tca<br>Ser        | gat<br>Asp        | ggt<br>Gly<br>370 | ctg<br>Leu        | cat<br>His        | gct<br>Ala        | gag<br>Glu        | gtt<br>Val<br>375 | act<br>Thr         | gga<br>Gly        | gtt<br>Va!        | ggc<br>Gly        | tat<br>Tyr<br>380 | aat<br>Asn        | caa<br>Gln        | 1572 |
| ttt<br>Phe        | ggg<br>Gly        | gaa<br>Glu<br>385 | gtg<br>Val        | att<br>Ile        | gtt<br>Val        | gat<br>Asp        | ggt<br>Gly<br>390 | gat<br>Asp        | gtt<br><b>Va</b> l | gtt<br>Val        | cat<br>His        | gga<br>Gly<br>395 | ttc<br>Phe        | tat<br>Tyr        | aac<br>Asn        | 1620 |
| cca<br>Pro        | gct<br>Ala<br>400 | gtt<br>Val        | agc<br>Ser        | aga<br>Arg        | att<br>lle        | gtt<br>Val<br>405 | gag<br>Glu        | gcg<br>Ala        | ggc<br>Gly         | tgt<br>Cys        | gtg<br>Val<br>410 | tgc<br>Cys        | aat<br>Asn        | gat<br>Asp        | gct<br>Ala        | 1668 |
| gta<br>Val<br>415 | att<br>Ile        | aga<br>Arg        | aac<br>Asn        | aat<br>Asn        | act<br>Thr<br>420 | cta<br>Leu        | atg<br>Met        | ggg<br>Gly        | aag<br>Lys         | cca<br>Pro<br>425 | aca<br>Thr        | gaa<br>Glu        | ggg<br>Gly        | gcc<br>Ala        | tta<br>Leu<br>430 | 1716 |
| att<br>lle        | gct<br>Ala        | ctt<br>Leu        | gca<br>Ala        | atg<br>Met<br>435 | aag<br>Lys        | atg<br>Met        | ggt<br>Gly        | ctt<br>Leu        | gat<br>Asp<br>440  | gga<br>Gly        | ctt<br>Leu        | caa<br>G n        | caa<br>Gln        | gac<br>Asp<br>445 | tac<br>Tyr        | 1764 |
| atc<br>He         | aga<br>Arg        | aaa<br>Lys        | gct<br>Ala<br>450 | gaa<br>Glu        | tac<br>Tyr        | cct<br>Pro        | ttt<br>Phe        | agc<br>Ser<br>455 | tct<br>Ser         | gag<br>Glu        | caa<br>Gln        | aag<br>Lys        | tgg<br>Trp<br>460 | atg<br>Met        | gct<br>Ala        | 1812 |
| gtt<br>Val        | aag<br>Lys        | tgt<br>Cys<br>465 | gta<br>Val        | cac<br>His        | cga<br>Arg        | aca<br>Thr        | cag<br>Gln<br>470 | cag<br>Gln        | gac<br>Asp         | aga<br>Arg        | cca<br>Pro        | gag<br>Glu<br>475 | att<br>lle        | tgt<br>Cys        | ttt<br>Phe        | 1860 |
| Met               | aaa<br>Lys<br>480 | Gly               | Ala               | tac<br>Tyr        | Glu               | Gln               | Val               | He                | Lys                | Tyr               | Cys               | Thr               | aca<br>Thr        | tac<br>Tyr        | cag<br>Gln        | 1908 |
| agc<br>Ser<br>495 | Lys               | ggg<br>Gly        | cag<br>Gln        | acc<br>Thr        | ttg<br>Leu<br>500 | aca<br>Thr        | ctt<br>Leu        | act<br>Thr        | cag<br>Gln         | cag<br>Gln<br>505 | Gln               | aga<br>Arg        | gat<br>Asp        | gtg<br>Val        | tac<br>Tyr<br>510 | 1956 |
| caa<br>Gln        | caa<br>G n        | gag<br>Glu        | aag<br>Lys        | gca<br>Ala<br>515 | Arg               | atg<br>Met        | ggc<br>Gly        | tca<br>Ser        | gcg<br>Ala<br>520  | Gly               | ctc<br>Leu        | aga<br>Arg        | gtt<br>Val        | ctt<br>Leu<br>525 | gct<br>Ala        | 2004 |
| ttg<br>Leu        | gct<br>Ala        | tct<br>Ser        | ggt<br>Gly<br>530 | Pro               | gaa<br>Glu        | ctg<br>Leu        | gga<br>Gly        | cag<br>Gln<br>535 | Leu                | aca<br>Thr        | ttt<br>Phe        | ctt<br>Leu        | ggc<br>Gly<br>540 | Leu               | gtg<br>Val        | 2052 |
| gga<br>Gly        | atc               | att<br>lle<br>545 | : Asp             | cca<br>Pro        | cct<br>Pro        | aga<br>Arg        | act<br>Thr<br>550 | Gly               | gtg<br>Val         | aaa<br>Lys        | gaa<br>Glu        | gct<br>Ala<br>555 | Val               | aca<br>Thr        | aca<br>Thr        | 2100 |
| ctc               | att               | gcc               | tca               | gga               | gta               | tca               | ata               | aaa               | atg                | att               | act               | gga               | gat               | tca               | cag               | 2148 |

| Leu               | lle<br>560        | Ala                 | Ser               | Gly               |                   | Ser<br>565        | Пе                  | Lys               | Met               | He                | Thr<br>570        | Gly               |                   | Ser               | Gln               |      |
|-------------------|-------------------|---------------------|-------------------|-------------------|-------------------|-------------------|---------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| gag<br>Glu<br>575 | act<br>Thr        | gca<br>Ala          | gtt<br>Val        | gca<br>Ala        | atc<br>  e<br>580 | gcc<br>Ala        | agt<br>Ser          | cgt<br>Arg        | ctg<br>Leu        | gga<br>Gly<br>585 | ttg<br>Leu        | tat<br>Tyr        | tcc<br>Ser        | aaa<br>Lys        | act<br>Thr<br>590 | 2196 |
| tcc<br>Ser        | cag<br>Gln        | tca<br>Ser          | gtc<br>Val        | tca<br>Ser<br>595 | gga<br>Gly        | gaa<br>Glu        | gaa<br>Glu          | ata<br>Ile        | gat<br>Asp<br>600 | gca<br>Ala        | atg<br>Met        | gat<br>Asp        | gtt<br>Val        | cag<br>Gln<br>605 | cag<br>Gln        | 2244 |
| ctt<br>Leu        | tca<br>Ser        | caa<br>Gln          | ata<br>Ile<br>610 | gta<br>Val        | cca<br>Pro        | aag<br>Lys        | gtt<br>Val          | gca<br>Ala<br>615 | gta<br>Val        | ttt<br>Phe        | tac<br>Tyr        | aga<br>Arg        | gct<br>Ala<br>620 | agc<br>Ser        | cca<br>Pro        | 2292 |
| agg<br>Arg        | cac<br>His        | aag<br>Lys<br>625   | atg<br>Met        | aaa<br>Lys        | att<br>lle        | att<br>Ile        | aag<br>Lys<br>630   | tcg<br>Ser        | cta<br>Leu        | cag<br>Gln        | aag<br>Lys        | aac<br>Asn<br>635 | ggt<br>Gly        | tca<br>Ser        | gtt<br>Val        | 2340 |
| gta<br>Val        | gcc<br>Ala<br>640 | atg<br>Met          | aca<br>Thr        | gga<br>Gly        | gat<br>Asp        | gga<br>Gly<br>645 | gta<br>Val          | aat<br>Asn        | gat<br>Asp        | gca<br>Ala        | gtt<br>Val<br>650 | gct<br>Ala        | ctg<br>Leu        | aag<br>Lys        | gct<br>Ala        | 2388 |
| gca<br>Ala<br>655 | gac<br>Asp        | att<br>Ile          | gga<br>Gly        | gtt<br>Val        | gcg<br>Ala<br>660 | atg<br>Met        | ggc<br>Gly          | cag<br>G n        | act<br>Thr        | ggt<br>Gly<br>665 | aca<br>Thr        | gat<br>Asp        | gtt<br>Val        | tgc<br>Cys        | aaa<br>Lys<br>670 | 2436 |
| gag<br>Glu        | gca<br>Ala        | gca<br>Ala          | gac<br>Asp        | atg<br>Met<br>675 | atc<br>He         | cta<br>Leu        | gtg<br>Val          | gat<br>Asp        | gat<br>Asp<br>680 | gat<br>Asp        | ttt<br>Phe        | caa<br>Gln        | acc<br>Thr        | ata<br>Ile<br>685 | atg<br>Met        | 2484 |
| tct<br>Ser        | gca<br>Ala        | atc<br>lle          | gaa<br>Glu<br>690 | gag<br>G u        | ggt<br>Gly        | aaa<br>Lys        | ggg<br>Gly          | att<br>  e<br>695 | tat<br>Tyr        | aat<br>Asn        | aac<br>Asn        | att<br>He         | aaa<br>Lys<br>700 | aat<br>Asn        | ttc<br>Phe        | 2532 |
| gtt<br>Val        | aga<br>Arg        | ttc<br>Phe<br>705   | cag<br>Gln        | ctg<br>Leu        | agc<br>Ser        | acg<br>Thr        | agt<br>Ser<br>710   | ata<br>Ile        | gca<br>Ala        | gca<br>Ala        | tta<br>Leu        | act<br>Thr<br>715 | tta<br>Leu        | atc<br>lle        | tca<br>Ser        | 2580 |
| ttg<br>Leu        | gct<br>Ala<br>720 | Thr                 | tta<br>Leu        | atg<br>Met        | aac<br>Asn        | ttt<br>Phe<br>725 | cct<br>Pro          | aat<br>Asn        | cct<br>Pro        | ctc<br>Leu        | aat<br>Asn<br>730 | gcc<br>Ala        | atg<br>Met        | cag<br>Gln        | att<br>He         | 2628 |
| ttg<br>Leu<br>735 | Trp               | ato<br>Ile          | aat<br>Asn        | att<br>Ille       | att<br>Ile<br>740 | Met               | gat<br>Asp          | gga<br>Gly        | ccc<br>Pro        | cca<br>Pro<br>745 | Ala               | cag<br>Gln        | agc<br>Ser        | ctt<br>Leu        | gga<br>Gly<br>750 | 2676 |
| gta<br>Val        | gaa<br>Glu        | cca<br>Pro          | gtg<br>Val        | gat<br>Asp<br>755 | Lys               | gat<br>Asp        | gtc<br>Val          | att               | cgt<br>Arg<br>760 | Lys               | cct<br>Pro        | cct<br>Pro        | cgc<br>Arg        | aad<br>Asn<br>765 | tgg<br>Trp        | 2724 |
| aaa<br>Lys        | gac<br>Asp        | ago<br>Ser          | att<br>   e       | : Leu             | act<br>Thr        | aaa<br>Lys        | aac<br>Asr          | ttg<br>Leu<br>775 | ılle              | ctt<br>Leu        | aaa<br>Lys        | ata<br>   ata     | ctt<br>Leu<br>780 | Val               | tca<br>Ser        | 2772 |
| tca<br>Ser        | ata<br>Ile        | ato<br>: 11e<br>785 | :   e             | gtt<br>Val        | tgt<br>Cys        | ggg<br>Gly        | ; act<br>Thr<br>790 | · Lei             | ttt<br>Phe        | gto<br>Val        | tto<br>Phe        | tgg<br>Trp<br>795 | ) Arg             | gag<br>Glu        | g cta<br>ı Leu    | 2820 |

| Arg               | gac<br>Asp<br>800             | aat<br>Asn         | gtg<br>Val        | att<br>He         | aca<br>Thr        | cct<br>Pro<br>805 | cga<br>Arg        | gac<br>Asp        | aca<br>Thr        | aca<br>Thr        | atg<br>Met<br>810 | acc<br>Thr        | ttc<br>Phe        | aca<br>Thr        | -0-               | 2868 |
|-------------------|-------------------------------|--------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| ttt<br>Phe<br>815 | gtg<br>Val                    | ttt<br>Phe         | ttt<br>Phe        | gac<br>Asp        | atg<br>Met<br>820 | ttc<br>Phe        | aat<br>Asn        | gca<br>Ala        | cta<br>Leu        | agt<br>Ser<br>825 | tcc<br>Ser        | aga<br>Arg        | tcc<br>Ser        | cag<br>Gln        | acc<br>Thr<br>830 | 2916 |
| aag<br>Lys        | tct<br>Ser                    | gtg<br>Val         | ttt<br>Phe        | gag<br>Glu<br>835 | att<br>Ile        | gga<br>Gly        | ctc<br>Leu        | tgc<br>Cys        | agt<br>Ser<br>840 | aat<br>Asn        | aga<br>Arg        | atg<br>Met        | ttt<br>Phe        | tgc<br>Cys<br>845 | tat<br>Tyr        | 2964 |
| gca<br>Ala        | gtt<br>Val                    | ctt<br>Leu         | gga<br>Gly<br>850 | tcc<br>Ser        | atc<br>.lle       | atg<br>Met        | gga<br>Gly        | caa<br>Gln<br>855 | tta<br>Leu        | cta<br>Leu        | gtt<br>Val        | att<br>Ile        | tac<br>Tyr<br>860 | ttt<br>Phe        | cct<br>Pro        | 3012 |
| ccg<br>Pro        | ctt<br>Leu                    | cag<br>Gln<br>865  | aag<br>Lys        | gtt<br>Val        | ttt<br>Phe        | cag<br>G n        | act<br>Thr<br>870 | gag<br>Glu        | agc<br>Ser        | cta<br>Leu        | agc<br>Ser        | ata<br>Ile<br>875 | ctg<br>Leu        | gat<br>Asp        | ctg<br>Leu        | 3060 |
| ttg<br>Leu        | ttt<br>Phe<br>880             | Leu                | ttg<br>Leu        | ggt<br>Gly        | ctc<br>Leu        | acc<br>Thr<br>885 | Ser               | tca<br>Ser        | gtg<br>Val        | tgc<br>Cys        | ata<br>Ile<br>890 | ۷a۱               | gca<br>Ala        | gaa<br>Glu        | att<br>Ile        | 3108 |
| ata<br>Ile<br>895 | Lys                           | aag<br>Lys         | gtt<br>Val        | gaa<br>Glu        | agg<br>Arg<br>900 | Ser               | agg<br>Arg        | gaa<br>Glu        | aag<br>Lys        | atc<br>Ile<br>905 | uin               | aag<br>Lys        | cat<br>His        | gtt<br>Val        | agt<br>Ser<br>910 | 3156 |
| tcg<br>Ser        | aca<br>Thr                    | tca<br>Ser         | tca<br>Ser        | tct<br>Ser<br>915 | Phe               | ctt<br>Leu        | gaa<br>Glu        | gta<br>Val        | tga               | tgca              | tat               | tgca              | ttat              | tt                |                   | 3203 |
| tat               | ttgc                          | aaa                | ctag              | gaat              | tg c              | agtc              | tgag              | g at              | catt              | taga              | agg               | gcaa              | gtt               | caag              | aggata            | 3263 |
|                   |                               |                    |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | aaagac            |      |
|                   |                               |                    |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | tattcc            |      |
|                   |                               |                    |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | ttattt            |      |
|                   |                               |                    |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | caaata            |      |
| cac               | tato                          | ctat               | ctta              | ngata             | iga t             | atat              | tttt              | t tt              | tatt              | ttta              | a aat             | attg              | gtac              | tatt              | tatggt            | 3563 |
| ggt               | gggg                          | gctt               | tctt              | acta              | aat a             | acaca             | aaata             | aa at             | tttaa             | atca              | t tto             | caaag             | ggc               |                   |                   | 3612 |
| <21<br><21<br><2  |                               | 382<br>PRT<br>Homo | sap               | iens              |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |      |
| Met               | 00><br>t GI <sup>-</sup><br>1 | 135<br>y Ala       | a Phe             |                   | u Ası<br>ō        | o Ly:             | s Pro             | o Ly:             | s Me              | t Gl              | u Ly              | s His             | s Ası             | n Ala             | a Gln<br>5        |      |



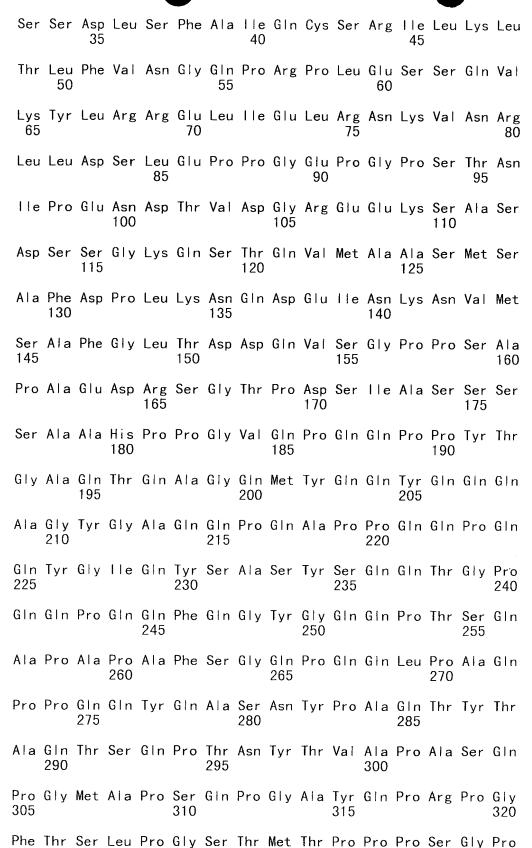
| Leu Ala Ser Glu Asn Ile Pro Ser Leu Pro Pro Gly Gly Glu Leu Ala 340 345 350  |
|--|
| Ser Lys Arg Asn Val IIe Glu Ala Val Tyr Asn Arg Leu Asn Pro Tyr<br>355 360 365   |
| Lys Asn Asp Asp Thr Asp Ser Thr Ser Thr Asp Asp Met Trp<br>370 375 380   |
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| tctagacagc tgaggcgcga aagcgatgag tcctcggctc ttcctcctcc ttctccggga 180  |
| cccgctctct gcctccctct ccaacgcccg gatgatctga gccgcgaggg cgccgacagc 240  |
| cgggggcccg gacgcagccc ggctcctccc ctcctccgcc ccttccccag cctgacctgg 300  |
| cccgccgctg cagcggtgac ccctccccg gctgccgccg tcgccgccgc ggtgacccc 360  |
| tecceggetg eegeegeege egeeteggee gaceagggae etgecegeet geggetgete 420  |
| cggacctaga ggatcaagac ata atg gga gca ttt tta gac aag cca aag atg 473<br>Met Gly Ala Phe Leu Asp Lys Pro Lys Met<br>1 5 10                         |
| gaa aag cat aat gcc cag ggg cag ggt aat ggg ttg cga tat ggg cta 521<br>Glu Lys His Asn Ala Gln Gly Gln Gly Asn Gly Leu Arg Tyr Gly Leu<br>15 20 25 |
| agc agc atg caa ggc tgg cgt gtt gaa atg gag gat gca cat acg gct 569<br>Ser Ser Met Gln Gly Trp Arg Val Glu Met Glu Asp Ala His Thr Ala<br>30 35 40 |
| gtg atc ggt ttg cca agt gga ctt gaa tcg tgg tca ttc ttt gct gtg Val lle Gly Leu Pro Ser Gly Leu Glu Ser Trp Ser Phe Phe Ala Val 45 50 55           |
| tat gat ggg cat gct ggt tct cag gtt gcc aaa tac tgc tgt gag cat Tyr Asp Gly His Ala Gly Ser Gln Val Ala Lys Tyr Cys Cys Glu His 60 65 70           |

ttg tta gat cac atc acc aat aac cag gat ttt aaa ggg tct gca gga Leu Leu Asp His IIe Thr Asn Asn Gln Asp Phe Lys Gly Ser Ala Gly

|     |     |     |     |     |     | gta<br>Val        |     |     |     |     |     |     |     |     |     | 761   |
|-----|-----|-----|-----|-----|-----|-------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------|
|     |     |     |     |     |     | aga<br>Arg        |     |     |     |     |     |     |     |     |     | 809   |
|     |     |     |     |     |     | gct<br>Ala        |     |     |     |     |     |     |     |     |     | 857   |
|     |     |     |     |     |     | gga<br>Gly<br>145 |     |     |     |     |     |     |     |     |     | 905   |
|     |     |     |     |     |     | aca<br>Thr        |     |     |     |     |     |     |     |     |     | 953   |
|     |     |     |     |     |     | aat<br>Asn        |     |     |     |     |     |     |     |     |     | 1001  |
|     |     |     |     |     |     | gta<br>Val        |     |     |     |     |     |     |     |     |     | 1049  |
|     |     |     |     |     |     | ggt<br>Gly        |     |     |     |     |     |     |     |     |     | 1097. |
|     |     |     |     |     |     | gaa<br>Glu<br>225 |     |     |     |     |     |     |     |     |     | 1145  |
|     |     |     |     |     |     | atc<br>lle        |     |     |     |     |     |     |     |     |     | 1193  |
|     |     |     |     |     |     | aga<br>Arg        |     |     |     |     |     |     |     |     |     | 1241  |
|     |     |     |     |     |     | gac<br>Asp        |     |     |     |     |     |     |     |     |     | 1289  |
|     |     |     |     |     |     | atc<br>Ile        |     |     |     |     |     |     |     |     |     | 1337  |
|     |     |     |     |     |     | gag<br>Glu<br>305 |     |     |     |     |     |     |     |     |     | 1385  |
| aga | gta | gaa | gaa | atc | ata | aag               | aag | cag | ggg | gaa | ggc | gtc | ссс | gac | tta | 1433  |

Arg Val Glu Glu IIe e Lys Lys Gln Gly Glu Gly Val P 315 330 gtc cat gtg atg cgc aca tta gcg agt gag aac atc ccc agc ctc cca 1481 Val His Val Met Arg Thr Leu Ala Ser Glu Asn Ile Pro Ser Leu Pro 335 cca ggg ggt gaa ttg gca agc aag agg aat gtt att gaa gcc gtt tac 1529 Pro Gly Gly Glu Leu Ala Ser Lys Arg Asn Val lle Glu Ala Val Tyr 350 aat aga ctg aat cct tac aaa aat gac gac act gac tct aca tca aca 1577 Asn Arg Leu Asn Pro Tyr Lys Asn Asp Asp Thr Asp Ser Thr Ser Thr 370 375 gat gat atg tgg taaaactgct catctagcca tggagtttac cttcacctcc 1629 Asp Asp Met Trp 380 aaaggagagt acagctcaac tttgttgaaa cttttaacat ccatcctcaa ctttaaggaa 1689 ggggatatga catgggtgag aatgattaca tcagagaact tcagcagtac aacagctagc 1749 ccagaactga ttttttttt ttttttgtaa atttgagact tatgtaagcg tgatttcaaa 1809 ccataattcg tgttgtaaat cagactccag caatttttgt tgtatgattt tgtttttttg 1869 taaagtgtaa ttgtccttgt acaaaatgct catatttaat tatgaactgc tttaaatcac 1929 tatcaaagtt acaagaaatg tttggcttat tgtgtgatgc aacagatata tagccctttc 1989 aagtcatgtt gtgtttggac ttggggttgg aacagggaga gcagcagcca tgtcagctac 2049 acgeteaaat gtgeagatga ttatggaaaa taaceteaaa atettacaaa getgaacate 2109 caaggagtta ttgaaaacta tottaaatgt tottggtagg ggagttggca ttgttgataa 2169 agocagtoco ttoatttaao tgtotttoag gatgttoott ogttgtttoo atgagtattg 2229 caggtaataa tacagtgtat tcataagaat ctcaatcttg gggctaaatg ccttgtttct 2289 ttgcacctct tttcaagtcc ttacatttaa ttactaattg ataagcagca gcttcctaca 2349 tatagtagga aactgccaca tttttgctat catgattggc tgggcctgct gctgttccta 2409 gtaagatatt ctgaattcca ttttatcaat aaagcttgat ttaacaaaca agaaactt <210> 137 <211> 358 <212> PRT <213> Homo sapiens <400> 137 Met Met Gln Arg Val Phe Arg Gly Lys Leu Leu Ser Asn Asp Glu Val

Thr lle Lys Tyr Lys Asp Glu Asp Gly Asp Leu lle Thr lle Phe Asp



Asn Pro Tyr Ala Arg Asn Arg Pro Pro Phe Gly Gln Gly Tyr Thr Gln 340 350

Pro Gly Pro Gly Tyr Arg 355

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| ccc agt gct cct gca gat cgt tca gga aca ccc gac agt tt gct Pro Ser Ala Pro Ala GTu Asp Arg Ser Gly Thr Pro Asp Ser Ile Ala 160 170                    | 529  |
|---|------|
| tcc tcc tca gca gct cac cca cca ggc gtt cag cca cag cag cca<br>Ser Ser Ser Ser Ala Ala His Pro Pro Gly Val Gln Pro Gln Gln Pro<br>175 180 185         | 577  |
| cca tat aca gga gct cag act caa gca ggt cag atg tac caa cag tac<br>Pro Tyr Thr Gly Ala Gln Thr Gln Ala Gly Gln Met Tyr Gln Gln Tyr<br>190 195 200 205 | 625  |
| cag caa cag gcc ggc tat ggt gca cag cag ccg cag gct cca cct cag<br>Gln Gln Gln Ala Gly Tyr Gly Ala Gln Gln Pro Gln Ala Pro Pro Gln<br>210 215 220     | 673  |
| cag cct caa cag tat ggt att cag tat tca gca agc tat agt cag cag<br>Gin Pro Gin Gin Tyr Giy lie Gin Tyr Ser Ala Ser Tyr Ser Gin Gin<br>225 230 235     | 721  |
| act gga ccc caa caa cct cag cag ttc cag gga tat ggc cag caa cca<br>Thr Gly Pro Gln Gln Pro Gln Gln Phe Gln Gly Tyr Gly Gln Gln Pro<br>240 245 250     | 769  |
| act too cag goa coa got cot goo tit tot ggt cag cot caa caa ctg<br>Thr Ser Gin Ala Pro Ala Pro Ala Phe Ser Giy Gin Pro Gin Gin Leu<br>255 260 265     | 817  |
| cct gct cag ccg cca cag cag tac cag gcg agc aat tat cct gca caa<br>Pro Ala Gln Pro Pro Gln Gln Tyr Gln Ala Ser Asn Tyr Pro Ala Gln<br>270 275 280 285 | 865  |
| act tac act gcc caa act tct cag cct act aat tat act gtg gct cct<br>Thr Tyr Thr Ala Gln Thr Ser Gln Pro Thr Asn Tyr Thr Val Ala Pro<br>290 295 300     | 913  |
| gcc tct caa cct gga atg gct cca agc caa cct ggg gcc tat caa cca<br>Ala Ser Gln Pro Gly Met Ala Pro Ser Gln Pro Gly Ala Tyr Gln Pro<br>305 310 315     | 961  |
| aga cca ggt ttt act tca ctt cct gga agt acc atg acc cct cct cca<br>Arg Pro Gly Phe Thr Ser Leu Pro Gly Ser Thr Met Thr Pro Pro Pro<br>320 325 330     | 1009 |
| agt ggg cct aat cct tat gcg cgt aac cgt cct ccc ttt ggt cag ggc<br>Ser Gly Pro Asn Pro Tyr Ala Arg Asn Arg Pro Pro Phe Gly Gln Gly<br>335 340 345     | 1057 |
| tat acc caa cct gga cct ggt tat cga taaggaggct cctctacacc<br>Tyr Thr Gln Pro Gly Pro Gly Tyr Arg<br>350 355   | 1104 |
| aattaatgta gctgctagct attggcctcc caaaagactc cagtactatt ttaatttgta   | 1164 |
| ttgaagaagt tcagaaattt aaaagcagag catttttat gatatcattg ttggtgttaa  |      |
| ttgaaagtat aatttgctgg aacacaaaga ccaaaatgaa agtttttcc tccctgctta  |      |

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1 10 15

Leu Gly Glu Asp lie Arg Arg lie Pro lie His Asn Glu Asp lie Thr
20 25 30

Tyr Asp Glu Leu Val Leu Met Met Gln Arg Val Phe Arg Gly Lys Leu 35 40 45

Leu Ser Asn Asp Glu Val Thr lle Lys Tyr Lys Asp Glu Asp Gly Asp 50 55 60

Leu lle Thr lle Phe Asp Ser Ser Asp Leu Ser Phe Ala lle Gln Cys 65 70 75 80

Ser Arg IIe Leu Lys Leu Thr Leu Phe Val Asn Gly Gln Pro Arg Pro 85 90 95

Leu Glu Ser Ser Gin Val Lys Tyr Leu Arg Arg Glu Leu lle Glu Leu 100 105 110

Arg Asn Lys Val Asn Arg Leu Leu Asp Ser Leu Glu Pro Pro Gly Glu
115 120 125

Pro Gly Pro Ser Thr Asn Ile Pro Glu Asn Asp Thr Val Asp Gly Arg 130 135 140

Glu Glu Lys Ser Ala Ser Asp Ser Ser Gly Lys Gln Ser Thr Gln Val 145 150 155 160

Met Ala Ala Ser Met Ser Ala Phe Asp Pro Leu Lys Asn Gln Asp Glu 165 170 175

lle Asn Lys Asn Val Met Ser Ala Phe Gly Leu Thr Asp Asp Gln Val

Ser Gly Pro Pro Ser Ala Pro Ala Glu Asp Arg Ser Gly Thr Pro Asp 195 200 205

Ser Ile Ala Ser Ser Ser Ser Ala Ala His Pro Pro Gly Val Gln Pro 210 220

Gln Gln Pro Pro Tyr Thr Gly Ala Gln Thr Gln Ala Gly Gln Met Tyr



| Gln | Gln | Tyr | Gln | Gln | Gln | Ala | Gly | Tyr | Gly | Ala | Gln | Gln | Pro | Gln | Ala |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |

Pro Pro Gln Gln Pro Gln Gln Tyr Gly lle Gln Tyr Ser Ala Ser Tyr 260 265 270

Ser Gln Gln Thr Gly Pro Gln Gln Pro Gln Gln Phe Gln Gly Tyr Gly 275 280 285

Gln Gln Pro Thr Ser Gln Ala Pro Ala Pro Ala Phe Ser Gly Gln Pro 290 295 300

Pro Ala Gln Thr Tyr Thr Ala Gln Thr Ser Gln Pro Thr Asn Tyr Thr 325 330 335

Val Ala Pro Ala Ser Gln Pro Gly Met Ala Pro Ser Gln Pro Gly Ala 340 345 350

Tyr Gln Pro Arg Pro Gly Phe Thr Ser Leu Pro Gly Ser Thr Met Thr 355 360 365

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Gly Gln Gly Tyr Thr Gln Pro Gly Pro Gly Tyr Arg 385 390 395

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<220>

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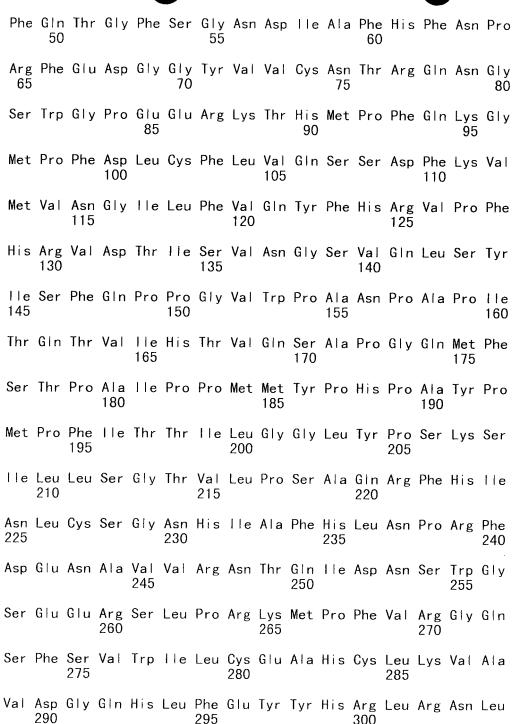
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|            | Glu        |                   |            |            |            |            |                   |            |            |            | Ser        | tct<br>Ser        |            |            |            | 243 |
|------------|------------|-------------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|-------------------|------------|------------|------------|-----|
|            |            |                   |            |            |            |            |                   |            |            | Leu        |            | tta<br>Leu        |            |            |            | 291 |
|            |            |                   |            |            |            |            |                   |            |            |            |            | tat<br>Tyr        |            |            |            | 339 |
| gaa<br>Glu | ctg<br>Leu | ata<br>  e<br>110 | gaa<br>Glu | ctt<br>Leu | cga<br>Arg | aat<br>Asn | aaa<br>Lys<br>115 | gtg<br>Val | aat<br>Asn | cgt<br>Arg | tta<br>Leu | ttg<br>Leu<br>120 | gat<br>Asp | agc<br>Ser | ttg<br>Leu | 387 |
|            |            |                   |            |            |            |            |                   |            |            |            |            | cct<br>Pro        |            |            |            | 435 |
|            |            |                   |            |            |            |            |                   |            |            |            |            | tct<br>Ser        |            |            |            | 483 |
|            |            |                   |            |            |            |            |                   |            |            |            |            | ttt<br>Phe        |            |            |            | 531 |
|            |            |                   |            |            |            |            |                   |            |            |            |            | gcg<br>Ala        |            |            |            | 579 |
|            |            |                   |            |            |            |            |                   |            |            |            |            | gca<br>Ala<br>200 |            |            |            | 627 |
|            |            |                   |            |            |            |            |                   |            |            |            |            | gca<br>Ala        |            |            |            | 675 |
|            |            |                   |            |            |            |            |                   |            |            |            |            | gct<br>Ala        |            |            |            | 723 |
|            |            |                   |            |            |            |            |                   |            |            |            |            | ggc<br>Gly        |            |            |            | 771 |
|            |            | Pro               |            |            |            |            | Gln               |            |            |            |            | tat<br>Tyr        |            |            |            | 819 |
|            | Ser        |                   |            |            |            | Gln        |                   |            |            |            |            | caa<br>Gln<br>280 |            |            |            | 867 |
| ttc        | cag        | gga               | tat        | ggc        | cag        | caa        | cca               | act        | tcc        | cag        | gca        | сса               | gct        | cct        | gcc        | 915 |

Phe Gln Gly Tyr Gly h Gln Pro Thr Ser Gln Ala Pro A 285 ttt tct ggt cag cct caa caa ctg cct gct cag ccg cca cag cag tac 963 Phe Ser Gly Gln Pro Gln Gln Leu Pro Ala Gln Pro Pro Gln Gln Tyr 300 310 cag gcg agc aat tat cct gca caa act tac act gcc caa act tct cag 1011 GIn Ala Ser Asn Tyr Pro Ala GIn Thr Tyr Thr Ala GIn Thr Ser GIn 325 cct act aat tat act gtg gct cct gcc tct caa cct gga atg gct cca 1059 Pro Thr Asn Tyr Thr Val Ala Pro Ala Ser Gln Pro Gly Met Ala Pro 335 340 agc caa cct ggg gcc tat caa cca aga cca ggt ttt act tca ctt cct 1107 Ser Gin Pro Gly Ala Tyr Gin Pro Arg Pro Gly Phe Thr Ser Leu Pro 355 gga agt acc atg acc cct cct cca agt ggg cct aat cct tat gcg cgt 1155 Gly Ser Thr Met Thr Pro Pro Pro Ser Gly Pro Asn Pro Tyr Ala Arg 365 370 aac cgt cct ccc ttt ggt cag ggc tat acc caa cct gga cct ggt tat 1203 Asn Arg Pro Pro Phe Gly Gln Gly Tyr Thr Gln Pro Gly Pro Gly Tyr 380 385 390 cga taaggaggct cctctacacc aattaatgta gctgctagct attggcctcc 1256 Arg caaaagactc cagtactatt ttaatttgta ttgaagaagt tcagaaattt aaaagcagag 1316 cattttttat gatatcattg ttggtgttaa ttgaaagtat aatttgctgg aacacaaaga 1376 ccaaaatgaa agtttttcc tccctgctta aaaatgtagc agcttcttag ttactttgga 1436 acactactct tacatgtata aagtgattga cttgactttc tagcttccct tgtccggagg 1496 atattaaaat gctagggtga ggtttagcca tcttacttgg ctttttacta ttaacatgat 1556 gtactaaagt agagcccttt gagaatacaa gatattatgt ataaaatgta acactgatga 1616 taggttaata aagatgattg aatcc 1641 <210> 141 <211> 323 <212> PRT <213> Homo sapiens <400> 141 Met Ala Phe Ser Gly Ser Gln Ala Pro Tyr Leu Ser Pro Ala Val Pro Phe Ser Gly Thr lle Gln Gly Gly Leu Gln Asp Gly Leu Gln lle Thr

Val Asn Gly Thr Val Leu Ser Ser Gly Thr Arg Phe Ala Val Asn



Val Gln Thr

315

Pro Thr lle Asn Arg Leu Glu Val Gly Gly Asp lle Gln Leu Thr His

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| gcggcggaga g atg g<br>Met A<br>1                  |   | cc cag gct ccc tac<br>er Gln Ala Pro Tyn<br>10 | r Leu Ser Pro                         |
| gct gtc ccc ttt tc<br>Ala Val Pro Phe Se<br>15    |   |  |                                       |
| cag atc act gtc aa<br>Gln lle Thr Val As<br>30    |   |  |                                       |
| gct gtg aac ttt ca<br>Ala Val Asn Phe Gli<br>50   | n Thr Gly Phe Sei                             |  |                                       |
| ttc aac cct cgg tt<br>Phe Asn Pro Arg Pho<br>65   | t gaa gat gga ggg<br>e Glu Asp Gly Gly<br>70  | / Tyr Val Val Cys                              | aac acg agg 302<br>Asn Thr Arg<br>75  |
| cag aac gga agc tgg<br>Gln Asn Gly Ser Trp<br>80  |   |  |                                       |
| cag aag ggg atg cco<br>Gln Lys Gly Met Pro<br>95  | c ttt gac ctc tgc<br>o Phe Asp Leu Cys<br>100 | ttc ctg gtg cag<br>Phe Leu Val Gln<br>105      | agc tca gat 398<br>Ser Ser Asp        |
| ttc aag gtg atg gtg<br>Phe Lys Val Met Va<br>110  | g aac ggg atc cto<br>Asn Gly lle Leu<br>115   | ttc gtg cag tac<br>Phe Val Gln Tyr<br>120      | ttc cac cgc 446<br>Phe His Arg<br>125 |
| gtg ccc ttc cac cgt<br>Val Pro Phe His Arg<br>130 | g Val Asp Thr ll $\epsilon$                   | tcc gtc aat ggc<br>Ser Val Asn Gly<br>135      | tct gtg cag 494<br>Ser Val Gln<br>140 |
| ctg tcc tac atc ago<br>Leu Ser Tyr lle Ser<br>145 | ttc cag cct ccc<br>Phe Gln Pro Pro<br>150     | Gly Val Trp Pro                                | gcc aac ccg 542<br>Ala Asn Pro<br>155 |
| gct ccc att acc cag<br>Ala Pro lle Thr Glr<br>160 | g aca gtc atc cac<br>n Thr Val Ile His<br>165 | aca gtg cag agc<br>Thr Val Gln Ser<br>170      | gcc cct gga 590<br>Ala Pro Gly        |
| cag atg ttc tct act<br>Gln Met Phe Ser Thr<br>175 | ccc gcc atc cca<br>Pro Ala IIe Pro<br>180     | cct atg atg tac<br>Pro Met Met Tyr<br>185      | ccc cac ccc 638<br>Pro His Pro        |

| gcc tat ccg atg cct ttc atc acc acc att ctg gga ggg ctg tac cca Ala Tyr Pro Met Pro Phe lle Thr Thr lle Leu Gly Gly Leu Tyr Pro 190 195 200 205           |   |
|---|---|
| tcc aag tcc atc ctc ctg tca ggc act gtc ctg ccc agt gct cag agg 734<br>Ser Lys Ser IIe Leu Leu Ser Gly Thr Val Leu Pro Ser Ala Gln Arg<br>210 215 220     |   |
| ttc cac atc aac ctg tgc tct ggg aac cac atc gcc ttc cac ctg aac 782 Phe His IIe Asn Leu Cys Ser Gly Asn His IIe Ala Phe His Leu Asn 225 230 235           |   |
| ccc cgt ttt gat gag aat gct gtg gtc cgc aac acc cag atc gac aac Pro Arg Phe Asp Glu Asn Ala Val Val Arg Asn Thr Gln Ile Asp Asn 240 245 250               |   |
| tcc tgg ggg tct gag gag cga agt ctg ccc cga aaa atg ccc ttc gtc 878<br>Ser Trp Gly Ser Glu Glu Arg Ser Leu Pro Arg Lys Met Pro Phe Val<br>255 260 265     |   |
| cgt ggc cag agc ttc tca gtg tgg atc ttg tgt gaa gct cac tgc ctc 926<br>Arg Gly Gln Ser Phe Ser Val Trp lle Leu Cys Glu Ala His Cys Leu<br>270 275 280 285 |   |
| aag gtg gcc gtg gat ggt cag cac ctg ttt gaa tac tac cat cgc ctg Lys Val Ala Val Asp Gly Gln His Leu Phe Glu Tyr Tyr His Arg Leu 290 295 300               |   |
| agg aac ctg ccc acc atc aac aga ctg gaa gtg ggg ggc gac atc cag Arg Asn Leu Pro Thr Ile Asn Arg Leu Glu Val Gly Gly Asp Ile Gln 305 310 315               |   |
| ctg acc cat gtg cag aca taggcggctt cctggccctg gggccggggg 1070<br>Leu Thr His Val Gln Thr<br>320   | ļ |
| ctggggtgtg gggcagtctg ggtcctctca tcatccccac ttcccaggcc cagcctttcc 1130  | ı |
| aaccctgcct gggatctggg ctttaatgca gaggccatgt ccttgtctgg tcctgcttct 1190  |   |
| ggctacagcc accetggaac ggagaaggca getgaegggg attgeettee teageegeag 1250  |   |
| cagcacctgg ggctccagct gctggaatcc taccatccca ggaggcaggc acagccaggg 1310  | 1 |
| agaggggagg agtgggcagt gaagatgaag ccccatgctc agtcccctcc catccccac 1370   | : |
| gcagctccac cccagtccca agccaccagc tgtctgctcc tggtgggagg tggcctcctc 1430  |   |
| agcccctcct ctctgacctt taacctcact ctcaccttgc accgtgcacc aacccttcac 1490  |   |
| ccctcctgga aagcaggcct gatggcttcc cactggcctc caccacctga ccagagtgtt 1550  |   |
| ctcttcagag gactggctcc tttcccagtg tccttaaaat aaagaaatga aaatgcttgt 1610  |   |
| tggcac 1616   |   |

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10

| ctg c                 | tc gt               | g ttc          | ca         | c          | atc        | gcc              | ttt        | ctg        | gtg        | gga        | ggc              |            | att        | gct        | 332  |
|-----------------------|---------------------|----------------|------------|------------|------------|------------------|------------|------------|------------|------------|------------------|------------|------------|------------|------|
| Leu L                 | eu Va               | Phe            | Gln<br>25  | lle        | He         | Āla              | Phe        | Leu<br>30  | Val        | Ğİy        | Ğİy              | Leu        | 11e<br>35  | Ala        |      |
| cca gg<br>Pro G       |                     |                |            |            |            |                  | Tyr        |            |            |            |                  |            |            |            | 380  |
|                       |                     | 40             |            |            |            |                  | 45         |            |            |            |                  | 50         |            |            |      |
| gcc ca<br>Ala A       | gt aa<br>rg Ly<br>5 | s Asn          | cat<br>His | cac<br>His | aag<br>Lys | aca<br>Thr<br>60 | aaa<br>Lys | tgg<br>Trp | ttc<br>Phe | gtg<br>Val | cct<br>Pro<br>65 | tgg<br>Trp | gga<br>Gly | ccc<br>Pro | 428  |
| aat ca<br>Asn H       |                     |                |            |            |            |                  |            |            |            |            |                  |            |            |            | 476  |
| att ga<br>lle G<br>85 |                     | c aat<br>a Asn |            |            |            |                  |            |            |            |            |                  |            |            |            | 524  |
| atg go<br>Met A       |                     |                |            |            |            |                  |            |            |            |            |                  |            |            |            | 572  |
| gtt tg<br>Val Cy      |                     |                |            |            |            |                  |            |            |            |            |                  |            |            |            | 620  |
| atg ca<br>Met Hi      |                     | s Val          | tgata      | ааса       | aa a       | acto             | tggt       | a tg       | gacac      | attt       | tct              | gtga       | atca       |            | 672  |
| ttgtta                | aatta               | gtgac          | atagt      | t aa       | cato       | tgta             | gca        | agcte      | gtt        | agta       | aacc             | ctc a      | atgtg      | gggggt     | 732  |
| ggggtg                | gggg                | tgtat          | tcctt      | gg         | ggga       | tggt             | ttg        | ggcc       | gaa        | tggg       | gagt             | gg a       | atat       | ttgac      | 792  |
| atttt                 | cctg                | tttta          | aatto      | ta         | ggat       | agat             | ttt        | aaca       | tcc        | tttg       | cggt             | cc c       | agto       | caagg      | 852  |
| taggct                | ggtg                | tcata          | gtctt      | ct         | cact       | ccta             | ato        | catg       | acc        | actg       | tttt             | tt t       | ccta       | tttat      | 912  |
| atcacc                | aggt                | agcct          | actga      | a gt       | taat       | attt             | aag        | ttgt       | саа        | taga       | itaag            | tg t       | ccct       | gtttt      | 972  |
| gtggca                | taat                | ataac          | tgaat      | : tt       | catg       | agaa             | gat        | ttat       | tcc        | acca       | gggg             | ta t       | ttca       | gcttt      | 1032 |
| gaaacc                | aaat                | ctgtg          | tatct      | aa         | tact       | аасс             | aat        | ctgt       | tgg        | atgt       | gggt             | tt t       | aaaa       | aatgt      | 1092 |
| ttgcta                | aact                | ассса          | agtaa      | a ga       | ttta       | ctgt             | att        | aaat       | ggc        | cttc       | gggt             | ct g       | gaaaa      | gcttt      | 1152 |
| tttaac                | ctct                | tgctt          | aaaat      | gc         | gttt       | tatt             | ttg        | ataa       | gat        | actt       | caaa             | ita g      | cctc       | саааа      | 1212 |
| gtgtag                | atcc                | aatca          | cttaa      | at         | aaac       | ctgt             | atg        | tata       | tgc        |            |                  |            |            |            | 1252 |

<210> 145 <211> 468 <212> PRT

<213> Homo sapiens

| <40        | 0> 1       | 45         |            |            |            |            |            |              |            |            |            |            |            |            |            |
|------------|------------|------------|------------|------------|------------|------------|------------|--------------|------------|------------|------------|------------|------------|------------|------------|
| Met<br>1   | Pro        | Val        | Arg        | Thr<br>5   |            | Thr        | Arg        | Gln          | Asn<br>10  |            | Ser        | Cys        | Leu        | Gly<br>15  | Asp        |
| Pro        | lle        | lle        | Va I<br>20 | Thr        | Arg        | Ser        | Glu        | Thr<br>25    | Leu        | Lys        | Arg        | Gln        | Phe<br>30  | Gln        | Phe        |
| Met        | Leu        | Phe<br>35  | lle        | Leu        | Gln        | Leu        | Asp<br>40  | He           | Ala        | Phe        | Lys        | Leu<br>45  | Asn        | Asn        | Glr        |
| He         | Arg<br>50  |            | Asn        | Ala        | Glu        | Val<br>55  | Ser        | Met          | Asp        | Val        | Ser<br>60  | Leu        | Ala        | Tyr        | Arg        |
| Asp<br>65  | Asp        | Ala        | Phe        | Ala        | Glu<br>70  | Trp        | Thr        | Glu          | Met        | Ala<br>75  | His        | Glu        | Arg        | Val        | Pro<br>80  |
| Arg        | Lys        | Leu        | Lys        | Cys<br>85  | Thr        | Phe        | Thr        | Ser          | Pro<br>90  | Lys        | Thr        | Pro        | Glu        | His<br>95  | Glu        |
| Gly        | Arg        | Tyr        | Tyr<br>100 | Glu        | Cys        | Asp        | Val        | Leu<br>105   | Pro        | Phe        | Met        | Glu        | 11e<br>110 | Gly        | Ser        |
| Val        | Ala        | His<br>115 | Lys        | Phe        | Tyr        | Leu        | Leu<br>120 | Asn          | lle        | Arg        | Leu        | Pro<br>125 | Val        | Asn        | Glu        |
| Lys        | Lys<br>130 | Lys        | lle        | Asn        | Val        | Gly<br>135 | lle        | Gly          | Glu        | lle        | Lys<br>140 | Asp        | lle        | Arg        | Leu        |
| Val<br>145 | Gly        | He         | His        | Gln        | Asn<br>150 | Gly        | Gly        | Phe          | Thr        | Lys<br>155 | Val        | Trp        | Phe        | Ala        | Met<br>160 |
| Lys        | Thr        | Phe        | Leu        | Thr<br>165 | Pro        | Ser        | lle        | Phe          | 11e<br>170 | lle        | Met        | Val        | Trp        | Tyr<br>175 | Trp        |
| Arg        | Arg        | lle        | Thr<br>180 | Met        | Met        | Ser        | Arg        | Pro<br>185   | Pro        | Val        | Leu        | Leu        | Glu<br>190 | Lys        | Val        |
| lle        | Phe        | Ala<br>195 | Leu        | Gly        | He         | Ser        | Met<br>200 | Thr          | Phe        | He         | Asn        | 11e<br>205 | Pro        | Val        | Glu        |
| Trp        | Phe<br>210 | Ser        | lle        | Gly        | Phe        | Asp<br>215 | Trp        | Thr          | Trp        | Met        | Leu<br>220 | Leu        | Phe        | Gly        | Asp        |
| 11e<br>225 | Arg        | Gln        | Gly        | lle        | Phe<br>230 | Tyr        | Ala        | Met          | Leu        | Leu<br>235 | Ser        | Phe        | Trp        | lle        | 11e<br>240 |
| Phe        | Cys        | Gly        | Glu        | His<br>245 | Met        | Met        | Asp        | Gln          | His<br>250 | Glu        | Arg        | Asn        | His        | 11e<br>255 | Ala        |
| Gly        | Tyr        | Trp        | Lys<br>260 | Gin        | Val        | Gly        | Pro        | 1 l e<br>265 | Ala        | Val        | Gly        | Ser        | Phe<br>270 | Cys        | Leu        |
| Phe        | lle        | Phe<br>275 | Asp        | Met        | Cys        | Glu        | Arg<br>280 | Gly          | Val        | Gln        | Leu        | Thr<br>285 | Asn        | Pro        | Phe        |
| Tyr        | Ser<br>290 | lle        | Trp        | Thr        |            | Asp<br>295 | lle        | Gly          | Thr        | Glu        | Leu<br>300 | Ala        | Met        | Ala        | Phe        |

lle lle Val Ala Gly e Cys Leu Cys Leu Tyr Phe Leu P 305 320 Phe Met Val Phe Gin Val Phe Arg Asn Ile Ser Gly Lys Gln Ser Ser 325 Leu Pro Ala Met Ser Lys Val Arg Arg Leu His Tyr Glu Gly Leu Ile 345 Phe Arg Phe Lys Phe Leu Met Leu IIe Thr Leu Ala Cys Ala Ala Met Thr Val He Phe Phe He Val Ser Gln Val Thr Glu Gly His Trp Lys 375 Trp Gly Gly Val Thr Val Gln Val Asn Ser Ala Phe Phe Thr Gly Ile 395 Tyr Gly Met Trp Asn Leu Tyr Val Phe Ala Leu Met Phe Leu Tyr Ala 415 Pro Ser His Lys Asn Tyr Gly Glu Asp Gln Ser Asn Gly Met Gln Leu 420 Pro Cys Lys Ser Arg Glu Asp Cys Ala Leu Phe Val Ser Glu Leu Tyr Gln Glu Leu Phe Ser Ala Ser Lys Tyr Ser Phe lle Asn Asp Asn Ala 450 Ala Ser Gly Ile 465 <210> 146 <211> 1943 <212> DNA <213> Homo sapiens <220> <221> CDS <222> (379).. (1782) <400> 146 acaatcacag ctccgggcat tgggggaacc cgagccggct gcgccggggg aatccgtgcg 60 ggcgccttcc gtcccggtcc catcctcgcc gcgctccagc acctctgaag ttttgcagcg 120 cccagaaagg aggcgaggaa ggagggagtg tgtgagagga gggagcaaaa agctcaccct 180 aaaacattta tttcaaggag aaaagaaaaa ggggggggcgc aaaaatggct ggggcaatta 240 tagaaaacat gagcaccaag aagctgtgca ttgttggtgg gattctgctc gtgttccaaa 300 tcatcgcctt tctggtggga ggcttgattg ctccagggcc cacaacggca gtgtcctaca 360 tgtcggtgaa atgtgtgg atg ccc gta aga acc atc aca aga caa aat ggt 411

Met Pro Val Arg Thr lle Thr Arg Gln Asn Gly

| tcg<br>Ser        | tgc<br>Cys        | ctt<br>Leu        | ggg<br>Gly<br>15  | Asp               | cca<br>Pro        | atc<br>lle        | att               | gtg<br>Val<br>20  | Thr               | aga<br>Arg        | toc<br>Ser        | gag<br>Glu        | aca<br>Thr<br>25  | Leu               | aag<br>Lys        | 459  |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| agg<br>Arg        | caa<br>Gln        | tto<br>Phe<br>30  | caa<br>Gln        | ttc<br>Phe        | atg<br>Met        | ctg<br>Leu        | ttt<br>Phe<br>35  | Пe                | ctg<br>Leu        | cag<br>Gln        | ctg<br>Leu        | gac<br>Asp<br>40  | att<br>He         | gcc<br>Ala        | ttc<br>Phe        | 507  |
| aag<br>Lys        | cta<br>Leu<br>45  | Asn               | aac<br>Asn        | caa<br>Gln        | atc<br>lle        | aga<br>Arg<br>50  | Glu               | aat<br>Asn        | gca<br>Ala        | gaa<br>Glu        | gtc<br>Val<br>55  | tcc<br>Ser        | atg<br>Met        | gac<br>Asp        | gtt<br>Val        | 555  |
| tcc<br>Ser<br>60  | Leu               | gct<br>Ala        | tac<br>Tyr        | cgt<br>Arg        | gat<br>Asp<br>65  | gac<br>Asp        | gcg<br>Ala        | ttt<br>Phe        | gct<br>Ala        | gag<br>Glu<br>70  | tgg<br>Trp        | act<br>Thr        | gaa<br>Glu        | atg<br>Met        | gcc<br>Ala<br>75  | 603  |
| cat<br>His        | gaa<br>Glu        | aga<br>Arg        | gta<br>Val        | cca<br>Pro<br>80  | cgg<br>Arg        | aaa<br>Lys        | ctc<br>Leu        | aaa<br>Lys        | tgc<br>Cys<br>85  | acc<br>Thr        | ttc<br>Phe        | aca<br>Thr        | tct<br>Ser        | ccc<br>Pro<br>90  | aag<br>Lys        | 651  |
| act<br>Thr        | cca<br>Pro        | gag<br>Glu        | cat<br>His<br>95  | gag<br>Glu        | ggc<br>Gly        | cgt<br>Arg        | tac<br>Tyr        | tat<br>Tyr<br>100 | gaa<br>Glu        | tgt<br>Cys        | gat<br>Asp        | gtc<br>Val        | ctt<br>Leu<br>105 | cct<br>Pro        | ttc<br>Phe        | 699  |
| atg<br>Met        | gaa<br>Glu        | att<br>He<br>110  | ggg<br>Gly        | tct<br>Ser        | gtg<br>Val        | gcc<br>Ala        | cat<br>His<br>115 | aag<br>Lys        | ttt<br>Phe        | tac<br>Tyr        | ctt<br>Leu        | tta<br>Leu<br>120 | aac<br>Asn        | atc<br>ile        | cgg<br>Arg        | 747  |
| ctg<br>Leu        | cct<br>Pro<br>125 | gtg<br>Val        | aat<br>Asn        | gag<br>Glu        | aag<br>Lys        | aag<br>Lys<br>130 | aaa<br>Lys        | atc<br>Ile        | aat<br>Asn        | gtg<br>Val        | gga<br>Gly<br>135 | att<br>He         | ggg<br>Gly        | gag<br>Glu        | ata<br>He         | 795  |
| aag<br>Lys<br>140 | gat<br>Asp        | atc<br>lle        | cgg<br>Arg        | ttg<br>Leu        | gtg<br>Val<br>145 | ggg<br>Gly        | atc<br>lle        | cac<br>His        | caa<br>G n        | aat<br>Asn<br>150 | gga<br>Gly        | ggc<br>Gly        | ttc<br>Phe        | acc<br>Thr        | aag<br>Lys<br>155 | 843  |
| gtg<br>Val        | tgg<br>Trp        | ttt<br>Phe        | gcc<br>Ala        | atg<br>Met<br>160 | aag<br>Lys        | acc<br>Thr        | ttc<br>Phe        | ctt<br>Leu        | acg<br>Thr<br>165 | ccc<br>Pro        | agc<br>Ser        | atc<br>lle        | ttc<br>Phe        | atc<br>lle<br>170 | att<br>lle        | 891  |
| atg<br>Met        | gtg<br>Val        | tgg<br>Trp        | tat<br>Tyr<br>175 | tgg<br>Trp        | agg<br>Arg        | agg<br>Arg        | atc<br>He         | acc<br>Thr<br>180 | atg<br>Met        | atg<br>Met        | tcc<br>Ser        | cga<br>Arg        | ccc<br>Pro<br>185 | cca<br>Pro        | gtg<br>Val        | 939  |
| ctt<br>Leu        | ctg<br>Leu        | gaa<br>Glu<br>190 | aaa<br>Lys        | gtc<br>Val        | atc<br>lle        | ttt<br>Phe        | gcc<br>Ala<br>195 | ctt<br>Leu        | ggg<br>Gly        | att<br>He         | tcc<br>Ser        | atg<br>Met<br>200 | acc<br>Thr        | ttt<br>Phe        | atc<br>  e        | 987  |
| Asn               | atc<br>lle<br>205 | cca<br>Pro        | gtg<br>Val        | gaa<br>Glu        | tgg<br>Trp        | ttt<br>Phe<br>210 | tcc<br>Ser        | atc<br>lle        | ggg<br>Gly        | Phe               | gac<br>Asp<br>215 | tgg<br>Trp        | acc<br>Thr        | tgg<br>Trp        | atg<br>Met        | 1035 |
| ctg<br>Leu<br>220 | ctg<br>Leu        | ttt<br>Phe        | ggt<br>Gly        | gac<br>Asp        | atc<br>Ile<br>225 | cga<br>Arg        | cag<br>Gln        | ggc<br>Gly        | Пe                | ttc<br>Phe<br>230 | tat<br>Tyr        | gcg<br>Ala        | atg<br>Met        | Leu               | ctg<br>Leu<br>235 | 1083 |

|                   |                   |                   |                   | 4                     |                   |                   |                   |                     |                       |                   |                   |                   |                   |                   |                   |      |
|-------------------|-------------------|-------------------|-------------------|-----------------------|-------------------|-------------------|-------------------|---------------------|-----------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| t co<br>Ser       | · Phe             | c tg;<br>e Tr;    | g ato<br>o IIo    | c at<br>e    c<br>240 | e Phe             | c tgt<br>e Cys    | t ggo<br>s Gly    | c gag<br>y Glu      | g cad<br>u His<br>245 | s Met             | g atg<br>: Met    | g gat<br>: Asp    | Glr               | cad<br>His<br>250 | gag<br>Glu<br>)   | 1131 |
| cgg<br>Arg        | g aad<br>g Asr    | cad<br>His        | 255               | e Ala                 | aggg<br>aGly      | g tat<br>/ Tyr    | tgg<br>Trp        | g aag<br>Lys<br>260 | s Glr                 | a gto<br>n Val    | gga<br>Gly        | ccc<br>Pro        | att<br>11e<br>265 | Ala               | gtt<br>Val        | 1179 |
| ggc<br>Gly        | tcc<br>Ser        | tto<br>Phe<br>270 | e Cys             | cto<br>Lei            | tto<br>Phe        | ata<br>e lle      | ttte Phe          | e Asp               | atg<br>Met            | g tgt<br>Cys      | gag<br>Glu        | aga<br>Arg<br>280 | Gly               | gta<br>Val        | caa<br>Gin        | 1227 |
| ctc<br>Leu        | acg<br>Thr<br>285 | Asr               | cco<br>Pro        | tto<br>Phe            | tac<br>Tyr        | agt<br>Ser<br>290 | lle               | tgg<br>Trp          | act<br>Thr            | aca<br>Thr        | gac<br>Asp<br>295 | Пe                | gga<br>Gly        | aca<br>Thr        | gag<br>Glu        | 1275 |
| ctg<br>Leu<br>300 | Ala               | atg<br>Met        | gcc<br>Ala        | tto<br>Phe            | atc<br>11e<br>305 | lle               | gtg<br>Val        | g gct<br>Ala        | gga<br>Gly            | atc<br>Ile<br>310 | Cys               | ctc<br>Leu        | tgc<br>Cys        | ctc<br>Leu        | tac<br>Tyr<br>315 | 1323 |
| ttc<br>Phe        | ctg<br>Leu        | ttt<br>Phe        | cta<br>Leu        | tgc<br>Cys<br>320     | Phe               | atg<br>Met        | gta<br>Val        | ttt<br>Phe          | cag<br>Gln<br>325     | Val               | ttt<br>Phe        | cgg<br>Arg        | aac<br>Asn        | atc<br>  e<br>330 | agt<br>Ser        | 1371 |
| ggg<br>Gly        | aag<br>Lys        | cag<br>G n        | tcc<br>Ser<br>335 | Ser                   | ctg<br>Leu        | cca<br>Pro        | gct<br>Ala        | atg<br>Met<br>340   | agc<br>Ser            | aaa<br>Lys        | gtc<br>Val        | cgg<br>Arg        | cgg<br>Arg<br>345 | cta<br>Leu        | cac<br>His        | 1419 |
| tat<br>Tyr        | gag<br>Glu        | ggg<br>Gly<br>350 | cta<br>Leu        | att<br>Ile            | ttt<br>Phe        | agg<br>Arg        | ttc<br>Phe<br>355 | aag<br>Lys          | ttc<br>Phe            | ctc<br>Leu        | atg<br>Met        | ctt<br>Leu<br>360 | atc<br>Ile        | acc<br>Thr        | ttg<br>Leu        | 1467 |
| gcc<br>Ala        | tgc<br>Cys<br>365 | gct<br>Ala        | gcc<br>Ala        | atg<br>Met            | act<br>Thr        | gtc<br>Val<br>370 | atc<br>lle        | ttc<br>Phe          | ttc<br>Phe            | atc<br>lle        | gtt<br>Val<br>375 | agt<br>Ser        | cag<br>Gln        | gta<br>Val        | acg<br>Thr        | 1515 |
| gaa<br>Glu<br>380 | Gly               | cat<br>His        | tgg<br>Trp        | Lys                   | tgg<br>Trp<br>385 | ggc<br>Gly        | ggc<br>Gly        | gtc<br>Val          | aca<br>Thr            | gtc<br>Val<br>390 | caa<br>Gln        | gtg<br>Val        | aac<br>Asn        | agt<br>Ser        | gcc<br>Ala<br>395 | 1563 |
| ttt<br>Phe        | ttc<br>Phe        | aca<br>Thr        | ggc<br>Gly        | atc<br>lle<br>400     | tat<br>Tyr        | ggg<br>Gly        | atg<br>Met        | tgg<br>Trp          | aat<br>Asn<br>405     | ctg<br>Leu        | tat<br>Tyr        | gtc<br>Val        | ttt<br>Phe        | gct<br>Ala<br>410 | ctg<br>Leu        | 1611 |
| atg<br>Met        | ttc<br>Phe        | ttg<br>Leu        | tat<br>Tyr<br>415 | gca<br>Ala            | cca<br>Pro        | tcc<br>Ser        | cat<br>His        | aaa<br>Lys<br>420   | aac<br>Asn            | tat<br>Tyr        | gga<br>Gly        | Glu               | gac<br>Asp<br>425 | cag<br>Gln        | tcc<br>Ser        | 1659 |
| aat<br>Asn        | Gly               | atg<br>Met<br>430 | caa<br>Gln        | ctc<br>Leu            | cca<br>Pro        | Cys               | aaa<br>Lys<br>435 | tcg<br>Ser          | agg<br>Arg            | gaa<br>Glu        |                   | tgt<br>Cys<br>440 | gct<br>Ala        | ttg<br>Leu        | ttt<br>Phe        | 1707 |
| gtt<br>Val        | tcg<br>Ser<br>445 | gaa<br>Glu        | ctt<br>Leu        | tat<br>Tyr            | Gln               | gaa<br>Giu<br>450 | ttg<br>Leu        | ttc<br>Phe          | agc<br>Ser            | Ala               | tcg<br>Ser<br>455 | aaa<br>Lys        | tat<br>Tyr        | tcc<br>Ser        | ttc<br>Phe        | 1755 |
| atc :             | aat<br>Asn        | gac<br>Asp        | aac<br>Asn        | gca<br>Ala            | gct<br>Ala        | tct<br>Ser        | ggt<br>Gly        | att<br>  e          | tgag                  | tcaa              | ca a              | ggca              | acac              | а                 |                   | 1802 |

tgtttatcag ctttgcattt gcagttgtca cagtcacatt gattgtactt gtatacgcac 1862 acaaatacac tcatttagcc tttatctcaa aatgttaaat ataaggaaaa aagcgtcaac 1922 aataaatatt ctttgagtat t

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Lys Leu Lys Pro Met Thr Ser Cys Phe Leu Phe Thr Phe Pro Ser Pro 35 40 45

Met Asp Val Ser Leu Ala Tyr Arg Asp Asp Ala Phe Ala Glu Trp Thr 50 55 60

Glu Met Ala His Glu Arg Val Pro Arg Lys Leu Lys Cys Thr Phe Thr 65 70 75 80

Ser Pro Lys Thr Pro Glu His Glu Gly Arg Tyr Tyr Glu Cys Asp Val 85 90 95

Leu Pro Phe Met Glu IIe Gly Ser Val Ala His Lys Phe Tyr Leu Leu 100 105 110

Asn lle Arg Leu Pro Val Asn Glu Lys Lys Lys lle Asn Val Gly lle 115 120 125

Gly Glu lle Lys Asp lle Arg Leu Val Gly lle His Gln Asn Gly Gly 130 135 140

Phe Thr Lys Val Trp Phe Ala Met Lys Thr Phe Leu Thr Pro Ser lle 145 150 155 160

Phe lle lle Met Val Trp Tyr Trp Arg Arg lle Thr Met Met Ser Arg 165 170 175

Pro Pro Val Leu Leu Glu Lys Val IIe Phe Ala Leu Gly IIe Ser Met 180 185 190

Thr Phe IIe Asn IIe Pro Val Glu Trp Phe Ser IIe Gly Phe Asp Trp 195 200 205

Thr Trp Met Leu Leu Phe Gly Asp lle Arg Gln Gly lle Phe Tyr Ala 210 215 220

Met Leu Leu Ser Phe Trp Ile lie Phe Cys Gly Glu His Met Met Asp

Gln His Glu Arg Asn His IIe Ala Gly Tyr Trp Lys Gln Val Gly Pro 245 250 255

lle Ala Val Gly Ser Phe Cys Leu Phe lle Phe Asp Met Cys Glu Arg 260 265 270

Gly Val Gln Leu Thr Asn Pro Phe Tyr Ser lle Trp Thr Thr Asp lle 275 280 285

Gly Thr Glu Leu Ala Met Ala Phe lle lle Val Ala Gly lle Cys Leu 290 295 300

Cys Leu Tyr Phe Leu Phe Leu Cys Phe Met Val Phe Gln Val Phe Arg 305 310 315 320

Asn Ile Ser Gly Lys Gln Ser Ser Leu Pro Ala Met Ser Lys Val Arg 325 330 335

Arg Leu His Tyr Glu Gly Leu lle Phe Arg Phe Lys Phe Leu Met Leu 340 345 350

lle Thr Leu Ala Cys Ala Ala Met Thr Val lle Phe Phe lle Val Ser 355 360 365

Gln Val Thr Glu Gly His Trp Lys Trp Gly Gly He Thr Val Gln Val 370 375 380

Asn Ser Ala Phe Phe Thr Gly lle Tyr Gly Met Trp Asn Leu Tyr Val 385 390 395 400

Phe Ala Leu Met Phe Leu Tyr Ala Pro Ser His Lys Asn Tyr Gly Glu 405 410 415

Asp Gln Ser Asn Gly Met Gln Leu Pro Cys Lys Ser Arg Glu Asp Cys 420 425 430

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| agaaaggagg cgaggaagga gggagtgtat gagaggaggg agcaaaaagc tcacctaaa   | 180 |
|--|-----|
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| aaaacatgag caccaagaag ctgtgcattg ttggtgggat tctgctcgtg ttccaaatca (  | 300 |
| tcgcctttct ggtgggaggc ttgattgctc cagggcccac aacggcagtg tcctacatgt (  | 360 |
| cggtgaaatg tgtgg atg ccc gta aga acc atc aca aga caa aat ggt tcg<br>Met Pro Val Arg Thr Ile Thr Arg Gln Asn Gly Ser<br>1 5 10                        | 411 |
| tgc ctt ggg gac cca atc att gtg aca aga tcc gag aca ttg aag agg<br>Cys Leu Gly Asp Pro IIe IIe Val Thr Arg Ser Glu Thr Leu Lys Arg<br>15 20 25       | 459 |
| caa ttc caa ggg aaa ttg aag cca atg aca tcg tgt ttt ctg ttc aca<br>Gln Phe Gln Gly Lys Leu Lys Pro Met Thr Ser Cys Phe Leu Phe Thr<br>30 35 40       | 507 |
| ttc ccc tcc ccc atg gac gtt tcc ctg gct tac cgt gat gac gcg ttt Phe Pro Ser Pro Met Asp Val Ser Leu Ala Tyr Arg Asp Asp Ala Phe 45 50 55 60          | 555 |
| gct gag tgg act gaa atg gcc cat gaa aga gta cca cgg aaa ctc aaa 6<br>Ala Glu Trp Thr Glu Met Ala His Glu Arg Val Pro Arg Lys Leu Lys<br>65 70 75     | 603 |
| tgc acc ttc aca tct ccc aag act cca gag cat gag ggc cgt tac tat 6<br>Cys Thr Phe Thr Ser Pro Lys Thr Pro Glu His Glu Gly Arg Tyr Tyr<br>80 85 90     | 651 |
| gaa tgt gat gtc ctt cct ttc atg gaa att ggg tct gtg gcc cat aag 6<br>Glu Cys Asp Val Leu Pro Phe Met Glu lie Gly Ser Val Ala His Lys<br>95 100 105   | 99  |
| ttt tac ctt tta aac atc cgg ctg cct gtg aat gag aag aag aaa atc 7<br>Phe Tyr Leu Leu Asn IIe Arg Leu Pro Val Asn Glu Lys Lys Lys IIe<br>110 115 120  | 47  |
| aat gtg gga att ggg gag ata aag gat atc cgg ttg gtg ggg atc cac 7 Asn Val Gly Ile Gly Glu Ile Lys Asp Ile Arg Leu Val Gly Ile His 125 130 135 140    | 95  |
| caa aat gga ggc ttc acc aag gtg tgg ttt gcc atg aag acc ttc ctt 8<br>Gln Asn Gly Gly Phe Thr Lys Val Trp Phe Ala Met Lys Thr Phe Leu<br>145 150 155  | 43  |
| acg ccc agc atc ttc atc att atg gtg tgg tat tgg agg agg atc acc 8 Thr Pro Ser lle Phe lle lle Met Val Trp Tyr Trp Arg Arg lle Thr 160 165 170        | 91  |
| atg atg tcc cga ccc cca gtg ctt ctg gaa aaa gtc atc ttt gcc ctt 9.<br>Met Met Ser Arg Pro Pro Val Leu Leu Glu Lys Val Ile Phe Ala Leu<br>175 180 185 | 39  |
| ggg att tcc atg acc ttt atc aat atc cca gtg gaa tgg ttt tcc atc 9  | 87  |

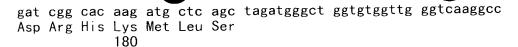
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|-----|------------|-----|-----|-----|-------------------|--------------|-----|-----|-----|-----|------------|-----|---|-----|-------------------|------|
|     |            |     |     |     | tgg<br>Trp<br>210 |              |     |     |     |     |            |     |   |     |                   | 1035 |
|     |            |     |     |     | ctt<br>Leu        |              |     |     |     |     |            |     |   |     |                   | 1083 |
|     |            |     |     |     | cac<br>His        |              |     |     |     |     |            |     |   |     |                   | 1131 |
|     |            |     |     |     | gcc<br>Ala        |              |     |     |     |     |            |     |   |     |                   | 1179 |
|     |            |     |     |     | gta<br>Val        |              |     |     |     |     |            |     |   |     |                   | 1227 |
|     |            |     |     |     | aca<br>Thr<br>290 |              |     |     |     |     |            |     |   |     |                   | 1275 |
|     |            |     |     |     | ctc<br>Leu        |              |     |     |     |     |            |     |   |     |                   | 1323 |
|     |            |     |     |     | atc<br>lle        |              |     |     |     |     |            |     |   |     |                   | 1371 |
|     |            |     |     |     | cta<br>Leu        |              |     |     |     |     |            |     |   |     |                   | 1419 |
|     |            |     |     |     | acc<br>Thr        |              |     |     |     |     |            |     |   |     |                   | 1467 |
|     |            |     |     |     | gta<br>Val<br>370 |              |     |     |     |     |            |     |   |     | atc<br>lle<br>380 | 1515 |
|     |            |     |     |     | agt<br>Ser        |              |     |     |     |     |            |     |   |     |                   | 1563 |
|     |            |     |     |     | gct<br>Ala        |              |     |     |     |     |            |     |   |     |                   | 1611 |
|     |            |     |     |     | cag<br>Gln        |              |     |     |     |     |            |     |   |     |                   | 1659 |

| agg gaa gat tgt gct ttg ttt gtt tcg gaa ctt tat caa gaa ttg<br>Arg Glu Asp Cys Ala Leu Phe Val Ser Glu Leu Tyr Gln Glu Leu F<br>430 435 440 | ttc 1707<br>Phe        |
|---|------------------------|
| agc gct tcg aaa tat tcc ttc atc aat gac aac gca gct tct ggt a<br>Ser Ala Ser Lys Tyr Ser Phe IIe Asn Asp Asn Ala Ala Ser Gly<br>445 450 455 | att 1755<br>lle<br>460 |
| tgagtcaaca aggcaacaca tgtttatcag ctttgcattt gcagttgtca cagtca   | acatt 1815             |
| gattgtactt gtatacgcac acaaatacac tcatttagcc tttatctcaa aatgtt   | taaat 1875             |
| ataaggaaaa aagcgtcaac aataaatatt ctttgagtat tgtc  | 1919                   |
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| Pro Ala Glu Ala Asn Lys Ser Ser Glu Asp Ile Arg Cys Lys Cys I<br>20 25 30   | le                     |
| Cys Pro Pro Tyr Arg Asn Ile Ser Gly His Ile Tyr Asn Gln Asn V<br>35 40 45   | al                     |
| Ser Gln Lys Asp Cys Asn Cys Leu His Val Val Glu Pro Met Pro V<br>50 55 60   | al                     |
| Pro Gly His Asp Val Glu Ala Tyr Cys Leu Leu Cys Glu Cys Arg Ty<br>65 70 75  | yr<br>80               |
| Glu Glu Arg Ser Thr Thr Thr Ile Lys Val Ile Ile Val Ile Tyr Le<br>85 90 95  | eu                     |
| Ser Val Val Gly Ala Leu Leu Leu Tyr Met Ala Phe Leu Met Leu Va<br>100 105 110   | al                     |
| Asp Pro Leu IIe Arg Lys Pro Asp Ala Tyr Thr Glu Gln Leu His As<br>115 120 125   | sn                     |
| Glu Glu Glu Asn Glu Asp Ala Arg Ser Met Ala Ala Ala Ala Ala Se<br>130 135 140   | er .                   |
| Leu Gly Gly Pro Arg Ala Asn Thr Vai Leu Glu Arg Val Glu Gly Al<br>145 150 155 16  |                        |
| Gin Gin Arg Trp Lys Leu Gin Val Gin Glu Gin Arg Lys Thr Val Ph<br>165 170 175   | ıe                     |

Asp Arg His Lys Met Leu Ser 180

| <2°               | 10> 1<br>11> 1<br>12> [<br>13> F | 1562<br>DNA       | sapi              | ens               |                   |                   |                   |                   |                   |                   |                   |                   |                   | <b>.</b>          |                   |     |
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| <22<br><22        |                                  | (120)             | (6                | 68)               |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |     |
|                   | )0> 1<br>eggct                   |                   | agaa              | gace              | gac a             | gaag              | ggga              | ıt ta             | agag              | ggag              | g ggc             | gggg              | gaca              | actg              | ggtcti            | 60  |
| ttg               | gegge                            | tgc               | agce              | ggct              | tg t              | aggt              | gtco              | g gc              | ttte              | ctgg              | ccc               | agca              | agc               | ctga              | taagc             | 119 |
| atg<br>Met<br>1   | g aag<br>: Lys                   | cto<br>Leu        | tta<br>Leu        | tct<br>Ser<br>5   | ttg<br>Leu        | gtg<br>Val        | gct<br>Ala        | gtg<br>Val        | gto<br>Val<br>10  | Gly               | tgt<br>Cys        | ttg<br>Leu        | ctg<br>Leu        | gtg<br>Val<br>15  | ccc<br>Pro        | 167 |
| cca<br>Pro        | gct<br>Ala                       | gaa<br>Glu        | gcc<br>Ala<br>20  | Asn               | aag<br>Lys        | agt<br>Ser        | tct<br>Ser        | gaa<br>Glu<br>25  | gat<br>Asp        | atc<br>lle        | cgg<br>Arg        | tgc<br>Cys        | aaa<br>Lys<br>30  | Cys               | atc<br>He         | 215 |
| tgt<br>Cys        | cca<br>Pro                       | cct<br>Pro<br>35  | lyr               | aga<br>Arg        | aac<br>Asn        | atc<br>Ile        | agt<br>Ser<br>40  | ggg<br>Gly        | cac<br>His        | att<br>lle        | tac<br>Tyr        | aac<br>Asn<br>45  | Gln               | aat<br>Asn        | gta<br>Val        | 263 |
| tcc<br>Ser        | cag<br>Gln<br>50                 | Lys               | gac<br>Asp        | tgc<br>Cys        | aac<br>Asn        | tgc<br>Cys<br>55  | ctg<br>Leu        | cac<br>His        | gtg<br>Val        | gtg<br>Val        | gag<br>Glu<br>60  | Pro               | atg<br>Met        | cca<br>Pro        | gtg<br>Val        | 311 |
| cct<br>Pro<br>65  | ggc<br>Gly                       | cat<br>His        | gac<br>Asp        | gtg<br>Val        | gag<br>Glu<br>70  | gcc<br>Ala        | tac<br>Tyr        | tgc<br>Cys        | ctg<br>Leu        | ctg<br>Leu<br>75  | tgc<br>Cys        | gag<br>Glu        | tgc<br>Cys        | agg<br>Arg        | tac<br>Tyr<br>80  | 359 |
| gag<br>Glu        | gag<br>Glu                       | cgc<br>Arg        | agc<br>Ser        | acc<br>Thr<br>85  | acc<br>Thr        | acc<br>Thr        | atc<br>lle        | aag<br>Lys        | gtc<br>Val<br>90  | atc<br>lle        | att<br>lie        | gtc<br>Val        | atc<br>lle        | tac<br>Tyr<br>95  | ctg<br>Leu        | 407 |
| tcc<br>Ser        | gtg<br>Val                       | gtg<br>Val        | ggt<br>Gly<br>100 | gcc<br>Ala        | ctg<br>Leu        | ttg<br>Leu        | ctc<br>Leu        | tac<br>Tyr<br>105 | atg<br>Met        | gcc<br>Ala        | ttc<br>Phe        | ctg<br>Leu        | atg<br>Met<br>110 | ctg<br>Leu        | gtg<br>Val        | 455 |
| gac<br>Asp        | cct<br>Pro                       | ctg<br>Leu<br>115 | atc<br>lle        | cga<br>Arg        | aag<br>Lys        | ccg<br>Pro        | gat<br>Asp<br>120 | gca<br>Ala        | tat<br>Tyr        | act<br>Thr        | gag<br>Glu        | caa<br>Gin<br>125 | ctg<br>Leu        | cac<br>His        | aat<br>Asn        | 503 |
| gag<br>Glu        | gag<br>Glu<br>130                | gag<br>Glu        | aat<br>Asn        | gag<br>Glu        | gat<br>Asp        | gct<br>Ala<br>135 | cgc<br>Arg        | tct<br>Ser        | atg<br>Met        | gca<br>Ala        | gca<br>Ala<br>140 | gct<br>Ala        | gct<br>Ala        | gca<br>Ala        | tcc<br>Ser        | 551 |
| ctc<br>Leu<br>145 | ggg<br>Gly                       | gga<br>Gly        | ccc<br>Pro        | cga<br>Arg        | gca<br>Ala<br>150 | aac<br>Asn        | aca<br>Thr        | gtc<br>Val        | ctg<br>Leu        | gag<br>Glu<br>155 | cgt<br>Arg        | gtg<br>Val        | gaa<br>Glu        | ggt<br>Gly        | gcc<br>Ala<br>160 | 599 |
| cag<br>Gln        | cag<br>Gln                       | cgg<br>Arg        | tgg<br>Trp        | aag<br>Lys<br>165 | ctg<br>Leu        | cag<br>Gln        | gtg<br>Val        | Gln               | gag<br>Glu<br>170 | cag<br>Gln        | cgg<br>Arg        | aag<br>Lys        | aca<br>Thr        | gtc<br>Val<br>175 | ttc<br>Phe        | 647 |

698



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|-------------------|------------|-------------------|-------------------|-------------------|-------------------|------------|-------------------|-------------------|-------------------|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-----|
|                   |            |                   |                   | gct<br>Ala<br>50  |                   |            |                   |                   |                   |                   |            |                   |                   |                   |                   | 374 |
|                   |            |                   |                   | atg<br>Met        |                   |            |                   |                   |                   |                   |            |                   |                   |                   |                   | 422 |
|                   |            |                   |                   | acc<br>Thr        |                   |            |                   |                   |                   |                   |            |                   |                   |                   |                   | 470 |
|                   |            |                   |                   | cgc<br>Arg        |                   |            |                   |                   |                   |                   |            |                   |                   |                   |                   | 518 |
| ccg<br>Pro<br>110 | gcc<br>Ala | tct<br>Ser        | aca<br>Thr        | agg<br>Arg        | gac<br>Asp<br>115 | atg<br>Met | gct<br>Ala        | tac<br>Tyr        | cag<br>Gln        | gtg<br>Val<br>120 | gcc<br>Ala | ctt<br>Leu        | cgt<br>Arg        | gac<br>Asp        | ttt<br>Phe<br>125 | 566 |
| gcc<br>Ala        | tcc<br>Ser | cag<br>Gln        | ggt<br>Gly        | gac<br>Asp<br>130 | cac<br>His        | cag<br>Gln | ctg<br>Leu        | ggc<br>Gly        | caa<br>Gln<br>135 | ctc<br>Leu        | cag<br>Gln | aat<br>Asn        | gag<br>Glu        | gcc<br>Ala<br>140 | tgg<br>Trp        | 614 |
|                   |            |                   |                   | tca<br>Ser        |                   |            |                   |                   |                   |                   |            |                   |                   |                   |                   | 662 |
| ctc<br>Leu        | cat<br>His | tct<br>Ser<br>160 | cat<br>His        | cag<br>Gln        | ggt<br>Gly        | tcc<br>Ser | ctg<br>Leu<br>165 | cag<br>G n        | cca<br>Pro        | cct<br>Pro        | tca<br>Ser | gca<br>Ala<br>170 | tcc<br>Ser        | cct<br>Pro        | gca<br>Ala        | 710 |
|                   |            |                   |                   | cag<br>Gln        |                   |            |                   |                   |                   |                   |            |                   |                   |                   |                   | 758 |
|                   |            |                   |                   | cac<br>His        |                   |            |                   |                   |                   |                   |            |                   |                   |                   |                   | 806 |
|                   |            |                   |                   | cag<br>Gln<br>210 |                   |            |                   |                   |                   |                   |            |                   |                   |                   |                   | 854 |
| gga<br>Gly        | acc<br>Thr | cat<br>His        | ggg<br>Gly<br>225 | ccc<br>Pro        | agc<br>Ser        | aag<br>Lys | cta<br>Leu        | tgt<br>Cys<br>230 | aac<br>Asn        | aca<br>Thr        | ccg<br>Pro | ctg<br>Leu        | gac<br>Asp<br>235 | act<br>Thr        | cag<br>Gln        | 902 |
|                   |            |                   |                   | gtc<br>Val        |                   |            |                   |                   |                   |                   |            |                   |                   |                   |                   | 950 |

|  |     |     |    |     |     |     |     |     |     | ggg<br>Gly<br>265 |     |     |  | 998  |
|--|-----|-----|----|-----|-----|-----|-----|-----|-----|-------------------|-----|-----|--|------|
|  |     |     |    |     |     |     |     |     |     | tcg<br>Ser        |     |     |  | 1046 |
|  |     |     |    |     |     |     |     |     |     | tgt<br>Cys        |     |     |  | 1094 |
|  |     |     |    |     |     |     |     |     |     | acg<br>Thr        |     |     |  | 1142 |
|  |     |     |    |     |     |     |     |     |     | agg<br>Arg        |     |     |  | 1190 |
|  |     |     |    |     |     |     |     |     |     | tca<br>Ser<br>345 |     |     |  | 1238 |
|  |     |     |    |     |     |     |     |     |     | ctg<br>Leu        |     |     |  | 1286 |
|  |     |     |    |     |     |     |     |     |     | gct<br>Ala        |     |     |  | 1334 |
|  |     |     |    |     |     |     |     |     |     | gat<br>Asp        |     |     |  | 1382 |
|  | Val | Val | He | His | Ala | Arg | Ala | Asp | Glu | cag<br>G n        | Val | Ala |  | 1430 |
|  |     |     |    |     |     |     |     |     |     | gac<br>Asp<br>425 |     |     |  | 1478 |
|  |     |     |    |     |     |     |     |     |     | ctg<br>Leu        |     |     |  | 1526 |
|  |     |     |    |     |     |     |     |     |     | ctc<br>Leu        |     |     |  | 1574 |
|  |     |     |    |     |     |     |     |     |     | cat<br>His        |     |     |  | 1622 |
|  |     |     |    |     |     |     |     |     |     | atc<br>He         |     |     |  | 1670 |

| ctt<br>Leu        | gag<br>Glu<br>495 | tgt<br>Cys        | tcc<br>Ser        | cag<br>Gln        | gcc<br>Ala        | cag<br>Gln<br>500 | ctc<br>Leu        | agc<br>Ser        | cca<br>Pro        | gat<br>Asp        | aca<br>Thr<br>505 | acc<br>Thr        | aga<br>Arg        | ctg<br>Leu        | ctc<br>Leu        | 1718 |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| cac<br>His<br>510 | agc<br>Ser        | att<br>Ile        | gtg<br>Val        | tgg<br>Trp        | ctg<br>Leu<br>515 | gat<br>Asp        | gaa<br>Glu        | cac<br>His        | tcc<br>Ser        | cca<br>Pro<br>520 | atc<br>Ile        | ttc<br>Phe        | gcc<br>Ala        | aga<br>Arg        | aag<br>Lys<br>525 | 1766 |
| gtg<br>Val        | gca<br>Ala        | aac<br>Asn        | acc<br>Thr        | ttc<br>Phe<br>530 | aag<br>Lys        | aca<br>Thr        | cag<br>Gln        | aag<br>Lys        | ctc<br>Leu<br>535 | cag<br>Gln        | gca<br>Ala        | cag<br>Gln        | cgg<br>Arg        | gta<br>Val<br>540 | cgc<br>Arg        | 1814 |
| tgg<br>Trp        | aag<br>Lys        | aaa<br>Lys        | gcg<br>Ala<br>545 | cag<br>Gln        | gag<br>Glu        | gcc<br>Ala        | aga<br>Arg        | acc<br>Thr<br>550 | ctc<br>Leu        | aag<br>Lys        | gag<br>G u        | cag<br>Gln        | agc<br>Ser<br>555 | ata<br>He         | cag<br>Gln        | 1862 |
| ctg<br>Leu        | gag<br>Glu        | gca<br>Ala<br>560 | gag<br>Glu        | cgg<br>Arg        | caa<br>Gln        | aac<br>Asn        | gtg<br>Val<br>565 | gca<br>Ala        | gcc<br>Ala        | ata<br>Ile        | tct<br>Ser        | gct<br>Ala<br>570 | gcc<br>Ala        | tac<br>Tyr        | aca<br>Thr        | 1910 |
| gcc<br>Ala        | tat<br>Tyr<br>575 | gtc<br>Val        | cat<br>His        | agc<br>Ser        | tat<br>Tyr        | agg<br>Arg<br>580 | gcc<br>Ala        | tgg<br>Trp        | caa<br>Gln        | gca<br>Ala        | gag<br>Glu<br>585 | atg<br>Met        | aac<br>Asn        | aaa<br>Lys        | ctt<br>Leu        | 1958 |
| ggg<br>Gly<br>590 | gtg<br>Val        | gct<br>Ala        | ttt<br>Phe        | ggg<br>Gly        | aag<br>Lys<br>595 | aac<br>Asn        | ttg<br>Leu        | tca<br>Ser        | ctg<br>Leu        | ggg<br>Gly<br>600 | act<br>Thr        | cca<br>Pro        | aca<br>Thr        | ccc<br>Pro        | agc<br>Ser<br>605 | 2006 |
| tgg<br>Trp        | ccc<br>Pro        | gga<br>Gly        | tgt<br>Cys        | cca<br>Pro<br>610 | cag<br>Gln        | cca<br>Pro        | ata<br>Ile        | cct<br>Pro        | tct<br>Ser<br>615 | cat<br>His        | cct<br>Pro        | cag<br>Gln        | ggt<br>Gly        | ggt<br>Gly<br>620 | act<br>Thr        | 2054 |
| cca<br>Pro        | gtt<br>Val        | ttc<br>Phe        | ccc<br>Pro<br>625 | tat<br>Tyr        | tcc<br>Ser        | cca<br>Pro        | cag<br>Gln        | cct<br>Pro<br>630 | cca<br>Pro        | tcc<br>Ser        | ttc<br>Phe        | cct<br>Pro        | cag<br>Gln<br>635 | cct<br>Pro        | cca<br>Pro        | 2102 |
| tgc<br>Cys        | ttc<br>Phe        | cct<br>Pro<br>640 | cag<br>Gln        | cct<br>Pro        | cca<br>Pro        | tcc<br>Ser        | ttc<br>Phe<br>645 | cct<br>Pro        | cag<br>Gln        | cct<br>Pro        | cca<br>Pro        | tcc<br>Ser<br>650 | ttc<br>Phe        | cca<br>Pro        | ctg<br>Leu        | 2150 |
| cct<br>Pro        | cca<br>Pro<br>655 | gtc<br>Val        | tct<br>Ser        | tcc<br>Ser        | cca<br>Pro        | cag<br>Gln<br>660 | tcc<br>Ser        | caa<br>Gln        | tcc<br>Ser        | ttt<br>Phe        | cca<br>Pro<br>665 | tca<br>Ser        | gcc<br>Ala        | tcc<br>Ser        | tcc<br>Ser        | 2198 |
| cca<br>Pro<br>670 | gcc<br>Ala        | cca<br>Pro        | cag<br>Gln        | act<br>Thr        | cca<br>Pro<br>675 | gga<br>Gly        | cct<br>Pro        | cag<br>Gln        | cct<br>Pro        | ctc<br>Leu<br>680 | att<br>Ile        | att<br>Ile        | cac<br>His        | cat<br>His        | gcc<br>Ala<br>685 | 2246 |
| cag<br>Gln        | atg<br>Met        | gtt<br>Val        | cag<br>Gln        | ctg<br>Leu<br>690 | ggt<br>Gly        | gtc<br>Val        | aac<br>Asn        | aat<br>Asn        | cac<br>His<br>695 | atg<br>Met        | tgg<br>Trp        | ggc<br>Gly        | cac<br>His        | aca<br>Thr<br>700 | ggg<br>Gly        | 2294 |
| gcc<br>Ala        | cag<br>Gln        | tca<br>Ser        | tct<br>Ser<br>705 | gat<br>Asp        | gac<br>Asp        | aag<br>Lys        | act<br>Thr        | gag<br>Glu<br>710 | tgt<br>Cys        | tcg<br>Ser        | gag<br>Glu        | aac<br>Asn        | ccc<br>Pro<br>715 | tgt<br>Cys        | atg<br>Met        | 2342 |

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<400> 152

Met Asp Asn Pro Gly Pro Ser Leu Arg Gly Ala Phe Gly Ile Leu Gly
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Leu Cys Ser Gly Ser Gln Glu Ser Lys Leu Leu His Ala Met Val Leu 35 40 45

Leu Ala Leu Gly Gln Asp Thr Glu Ala Arg Val Ser Leu Glu Ser Leu 50 60

Lys Met Asn Thr Val Ala Gln Leu Val Ala His Gln Trp Ala Asp Met 65 70 75 80

Glu Thr Thr Glu Gly Pro Glu Glu Pro Pro Asp Leu Ser Trp Thr Val 85 90 95

Ala Arg Leu Tyr His Leu Leu Ala Glu Glu Asn Leu Cys Pro Ala Ser 100 110

Thr Arg Asp Met Ala Tyr Gin Val Ala Leu Arg Asp Phe Ala Ser Gin 115 120 125

Gly Asp His Gln Leu Gly Gln Leu Gln Asn Glu Ala Trp Asp Arg Cys 130 135 140

Ser Ser Asp IIe Lys Gly Asp Pro Ser Gly Phe Gln Pro Leu His Ser 150 . 155

His Gln Gly Ser Leu Gln Pro Pro Ser Ala Ser Pro Ala Val Thr Arg





Ser Gln Pro Arg Pro IIe Asp Thr Pro Asp Trp Ser Trp Gly His Thr 180 185 190

Leu His Ser Thr Asn Ser Thr Ala Ser Leu Ala Ser His Leu Glu lle 195 200 205

Ser Gln Ser Pro Thr Leu Ala Phe Leu Ser Ser His His Gly Thr His 210 215 220

Gly Pro Ser Lys Leu Cys Asn Thr Pro Leu Asp Thr Gln Glu Pro Gln 225 230 235 240

Leu Vai Pro Glu Gly Cys Gln Glu Pro Glu Glu lle Ser Trp Pro Pro 245 250 255

Ser Val Glu Thr Ser Val Ser Leu Gly Leu Pro His Glu Ile Ser Val 260 265 270

Pro Glu Val Ser Pro Glu Glu Ala Ser Pro IIe Leu Pro Asp Ala Leu 275 280 285

Ala Ala Pro Asp Thr Ser Val His Cys Pro Ile Glu Cys Thr Glu Leu 290 295 300

Ser Thr Asn Ser Arg Ser Pro Leu Thr Ser Thr Thr Glu Ser Val Gly 305 310 315 320

Lys Gln Trp Pro Ile Thr Ser Gln Arg Ser Pro Gln Val Pro Val Gly 325 330 335

Asp Asp Ser Leu Gln Asn Thr Thr Ser Ser Ser Pro Pro Ala Gln Pro 340 350

Pro Ser Leu Gln Ala Ser Pro Lys Leu Pro Pro Ser Pro Leu Ser Ser 355 360 365

Ala Ser Ser Pro Ser Ser Tyr Pro Ala Pro Pro Thr Ser Thr Ser Pro 370 375 380

Val Leu Asp His Ser Glu Thr Ser Asp Gln Lys Phe Tyr Asn Phe Val 385 390 395 400

Val lle His Ala Arg Ala Asp Glu Gln Val Ala Leu Arg lle Arg Glu 405 410 415

Lys Leu Glu Thr Leu Gly Val Pro Asp Gly Ala Thr Phe Cys Glu Glu 420 425 430

Phe Gln Val Pro Gly Arg Gly Glu Leu His Cys Leu Gln Asp Ala Ile 435 440 445

Asp His Ser Gly Phe Thr lle Leu Leu Leu Thr Ala Ser Phe Asp Cys 450 455 460

Ser Leu Ser Leu His Gln Ile Asn His Ala Leu Met Asn Ser Leu Thr 465 470 475 480

Gln Ser Gly Arg Gln Asp Cys Val Ile Pro Leu Leu Pro Leu Glu Cys Ser Gln Ala Gln Leu Ser Pro Asp Thr Thr Arg Leu Leu His Ser lle 505 Val Trp Leu Asp Glu His Ser Pro Ile Phe Ala Arg Lys Val Ala Asn Thr Phe Lys Thr Gln Lys Leu Gln Ala Gln Arg Val Arg Trp Lys Lys Ala Gin Giu Ala Arg Thr Leu Lys Giu Gin Ser ile Gin Leu Giu Ala 545 555 Glu Arg Gln Asn Val Ala Ala Ile Ser Ala Ala Tyr Thr Ala Tyr Val 570 His Ser Tyr Arg Ala Trp Gln Ala Glu Met Asn Lys Leu Gly Val Ala 585 Phe Gly Lys Asn Leu Ser Leu Gly Thr Pro Thr Pro Ser Trp Pro Gly 595 600 605 Cys Pro Gln Pro lle Pro Ser His Pro Gln Gly Gly Thr Pro Val Phe Pro Tyr Ser Pro Gin Pro Pro Ser Phe Pro Gin Pro Pro Cys Phe Pro 635 Gln Pro Pro Ser Phe Pro Gln Pro Pro Ser Phe Pro Leu Pro Pro Val Ser Ser Pro Gln Ser Gln Ser Phe Pro Ser Ala Ser Ser Pro Ala Pro 665 Gin Thr Pro Gly Pro Gin Pro Leu Ile Ile His His Ala Gin Met Val 675 680 Gln Leu Gly Val Asn Asn His Met Trp Gly His Thr Gly Ala Gln Ser 695 Ser Asp Asp Lys Thr Glu Cys Ser Glu Asn Pro Cys Met Gly Pro Leu 710

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Thr Asp Gln Gly Glu Pro Leu Leu Glu Thr Pro Glu

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ago cot goo too otg goo ago aac ttg gaa ato ago cag too cot aco

| Ser               | Pro<br>200        | Ala               | Ser               | Leu               | a                 | Ser<br>205        | Asn               | Leu               | Glu               | lle               | Ser<br>210        | Gln               | 3                 | Pro               | Thr               |      |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| atg<br>Met<br>215 | ccc<br>Pro        | ttc<br>Phe        | ctc<br>Leu        | agc<br>Ser        | ctg<br>Leu<br>220 | cac<br>His        | cgc<br>Arg        | agc<br>Ser        | cca<br>Pro        | cat<br>His<br>225 | ggg<br>Gly        | ccc<br>Pro        | agc<br>Ser        | aag<br>Lys        | ctc<br>Leu<br>230 | 786  |
| tgt<br>Cys        | gac<br>Asp        | gac<br>Asp        | ccc<br>Pro        | cag<br>Gln<br>235 | gcc<br>Ala        | agc<br>Ser        | ttg<br>Leu        | gtg<br>Val        | ccc<br>Pro<br>240 | gag<br>Glu        | cct<br>Pro        | gtc<br>Val        | ccc<br>Pro        | ggt<br>Gly<br>245 | ggc<br>Gly        | 834  |
| tgc<br>Cys        | cag<br>Gln        | gag<br>Glu        | cct<br>Pro<br>250 | gag<br>Glu        | gag<br>Glu        | atg<br>Met        | agc<br>Ser        | tgg<br>Trp<br>255 | ccg<br>Pro        | cca<br>Pro        | tcg<br>Ser        | ggg<br>Gly        | gag<br>Glu<br>260 | att<br>He         | gcc<br>Ala        | 882  |
| agc<br>Ser        | cca<br>Pro        | cca<br>Pro<br>265 | gag<br>Glu        | ctg<br>Leu        | cca<br>Pro        | agc<br>Ser        | agc<br>Ser<br>270 | cca<br>Pro        | cct<br>Pro        | cct<br>Pro        | ggg<br>Gly        | ctt<br>Leu<br>275 | ccc<br>Pro        | gaa<br>Glu        | gtg<br>Val        | 930  |
| gcc<br>Ala        | cca<br>Pro<br>280 | gat<br>Asp        | gca<br>Ala        | acc<br>Thr        | tcc<br>Ser        | act<br>Thr<br>285 | ggc<br>Gly        | ctc<br>Leu        | cct<br>Pro        | gat<br>Asp        | acc<br>Thr<br>290 | ccc<br>Pro        | gca<br>Ala        | gct<br>Ala        | cca<br>Pro        | 978  |
| gaa<br>Glu<br>295 | acc<br>Thr        | agc<br>Ser        | acc<br>Thr        | aac<br>Asn        | tac<br>Tyr<br>300 | cca<br>Pro        | gtg<br>Val        | gag<br>Glu        | tgc<br>Cys        | acc<br>Thr<br>305 | gag<br>Glu        | ggg<br>Gly        | tct<br>Ser        | gca<br>Ala        | ggc<br>Gly<br>310 | 1026 |
| ccc<br>Pro        | cag<br>Gln        | tct<br>Ser        | ctc<br>Leu        | ccc<br>Pro<br>315 | ttg<br>Leu        | cct<br>Pro        | att<br>Ile        | ctg<br>Leu        | gag<br>Glu<br>320 | ccg<br>Pro        | gtc<br>Val        | aaa<br>Lys        | aac<br>Asn        | ccc<br>Pro<br>325 | tgc<br>Cys        | 1074 |
| tct<br>Ser        | gtc<br>Val        | aaa<br>Lys        | gac<br>Asp<br>330 | cag<br>G n        | acg<br>Thr        | cca<br>Pro        | ctc<br>Leu        | caa<br>Gln<br>335 | ctt<br>Leu        | tct<br>Ser        | gta<br>Val        | gaa<br>Glu        | gat<br>Asp<br>340 | acc<br>Thr        | acc<br>Thr        | 1122 |
| tct<br>Ser        | cca<br>Pro        | aat<br>Asn<br>345 | acc<br>Thr        | aag<br>Lys        | ccg<br>Pro        | tgc<br>Cys        | cca<br>Pro<br>350 | cct<br>Pro        | act<br>Thr        | ccc<br>Pro        | acc<br>Thr        | acc<br>Thr<br>355 | cca<br>Pro        | gaa<br>Glu        | aca<br>Thr        | 1170 |
|                   |                   |                   |                   | cct<br>Pro        |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | 1218 |
| cac<br>His<br>375 | ctg<br>Leu        | acc<br>Thr        | ccc<br>Pro        | tcc<br>Ser        | tcc<br>Ser<br>380 | ctg<br>Leu        | ttc<br>Phe        | cct<br>Pro        | tcc<br>Ser        | tcc<br>Ser<br>385 | ctg<br>Leu        | gaa<br>Glu        | tca<br>Ser        | tca<br>Ser        | tcg<br>Ser<br>390 | 1266 |
| gaa<br>Glu        | cag<br>Gln        | aaa<br>Lys        | ttc<br>Phe        | tat<br>Tyr<br>395 | aac<br>Asn        | ttt<br>Phe        | gtg<br>Val        | atc<br>Ile        | ctc<br>Leu<br>400 | cac<br>His        | gcc<br>Ala        | agg<br>Arg        | gca<br>Ala        | gac<br>Asp<br>405 | gaa<br>Glu        | 1314 |
| cac<br>His        | atc<br>Ile        | gcc<br>Ala        | ctg<br>Leu<br>410 | cgg<br>Arg        | gtt<br>Val        | cgg<br>Arg        | gag<br>Glu        | aag<br>Lys<br>415 | ctg<br>Leu        | gag<br>Glu        | gcc<br>Ala        | ctt<br>Leu        | ggc<br>Gly<br>420 | gtg<br>Val        | ccc<br>Pro        | 1362 |
| gac<br>Asp        | ggg<br>Gly        | gcc<br>Ala<br>425 | acc<br>Thr        | ttc<br>Phe        | tgc<br>Cys        | gag<br>Glu        | gat<br>Asp<br>430 | ttc<br>Phe        | cag<br>Gln        | gtg<br>Val        | ccg<br>Pro        | ggg<br>Gly<br>435 | cgc<br>Arg        | ggg<br>Gly        | gag<br>Glu        | 1410 |

|                   |            | Cys        | ctg<br>Leu        |                   |                   |            |            |            |                   |                   |            | Phe        |            |                   |                   | 1458   |
|-------------------|------------|------------|-------------------|-------------------|-------------------|------------|------------|------------|-------------------|-------------------|------------|------------|------------|-------------------|-------------------|--------|
| ctt<br>Leu<br>455 | ctc<br>Leu | acc<br>Thr | tcc<br>Ser        | aac<br>Asn        | ttc<br>Phe<br>460 | gac<br>Asp | tgt<br>Cys | cgc<br>Arg | ctg<br>Leu        | agc<br>Ser<br>465 | ctg<br>Leu | cac<br>His | cag<br>Gln | gtg<br>Val        | aac<br>Asn<br>470 | 1506   |
|                   |            |            | atg<br>Met        |                   |                   |            |            |            |                   |                   |            |            |            |                   |                   | 1554   |
|                   |            |            | ctg<br>Leu<br>490 |                   |                   |            |            |            |                   |                   |            |            |            |                   |                   | 1602   |
|                   |            |            | ctg<br>Leu        |                   |                   |            |            |            |                   |                   |            |            |            |                   |                   | 1650   |
|                   |            |            | agg<br>Arg        |                   |                   |            |            |            |                   |                   |            |            |            |                   |                   | 1698   |
|                   |            |            | gcc<br>Ala        |                   |                   |            |            |            |                   |                   |            |            |            |                   |                   | 1746   |
| gaa<br>Glu        | cag<br>Gln | agc<br>Ser | caa<br>Gln        | cac<br>His<br>555 | ctg<br>Leu        | gac<br>Asp | ggt<br>Gly | gag<br>Glu | cgg<br>Arg<br>560 | atg<br>Met        | cag<br>Gln | gcg<br>Ala | gcg<br>Ala | gca<br>Ala<br>565 | ctg<br>Leu        | 1794 . |
|                   |            |            | tac<br>Tyr<br>570 |                   |                   |            |            |            |                   |                   |            |            |            |                   |                   | 1842   |
|                   |            | Glu        | cag<br>G n        | Leu               | Gln               | Val        | Ala        | Phe        | Gly               | Ser               | His        | Met        | Ser        |                   |                   | 1890   |
|                   |            |            | ccc<br>Pro        |                   |                   |            |            |            |                   |                   |            |            |            |                   |                   | 1938   |
| ctg<br>Leu<br>615 | gga<br>Gly | gcc<br>Ala | ccg<br>Pro        | cca<br>Pro        | ccc<br>Pro<br>620 | ttt<br>Phe | ccc<br>Pro | act<br>Thr | tgg<br>Trp        | ccg<br>Pro<br>625 | ggg<br>Gly | tgc<br>Cys | ccg<br>Pro | cag<br>Gln        | ccg<br>Pro<br>630 | 1986   |
|                   |            |            | cac<br>His        |                   |                   |            |            |            |                   |                   |            |            |            |                   |                   | 2034   |
|                   |            |            | gcc<br>Ala<br>650 |                   |                   |            | Ser        |            |                   |                   |            |            |            |                   |                   | 2082   |
| ttc               | cct        | acg        | gcc               | tca               | ccc               | gca        | ccc        | cct        | cag               | agc               | сса        | ggg        | ctg        | caa               | ссс               | 2130   |

| Phe Pro Thr Ala Ser Ala Pro Pro Gln Ser Pro Gly Legiln Pro 665 670 675   |
|--|
| ctc att atc cac cac gca cag atg gta cag ctg ggg ctg aac aac cac 2178<br>Leu lle lle His His Ala Gln Met Val Gln Leu Gly Leu Asn Asn His<br>680 685 690     |
| atg tgg aac cag aga ggg tcc cag gcg ccc gag gac aag acg cag gag 2226<br>Met Trp Asn Gln Arg Gly Ser Gln Ala Pro Glu Asp Lys Thr Gln Glu<br>695 700 705 710 |
| gca gaa tgaccgcgtg tccttgcctg accacctggg gaacacccct ggacccaggc 2282<br>Ala Glu   |
| atcggccagg accccataga gcaccccggt ctgccctgtg ccctgtggac agtggaagat 2342   |
| gaggtcatct gccactttca ggacattgtc cgggagccct tcatttagga caaaacgggc 2402   |
| gcgatgatgc cctggctttc agggtggtca gaactggata cggtgtttac aattccaatc 2462   |
| tctctatttc tgggtgaagg gtcttggtgg tgggggtatt gctacggtct tttaattata 2522   |
| ataaatattt attgaatgct tc 2544  |
| <210> 154<br><211> 712<br><212> PRT<br><213> Homo sapiens  |
| <pre>&lt;400&gt; 154 Met Ala Cys Thr Gly Pro Ser Leu Pro Ser Ala Phe Asp lle Leu Gly 1</pre>   |
| Ala Ala Gly Gln Asp Lys Leu Leu Tyr Leu Lys His Lys Leu Lys Thr<br>20 25 30  |
| Pro Arg Pro Gly Cys Gln Gly Gln Asp Leu Leu His Ala Met Val Leu<br>35 40 45  |
| Leu Lys Leu Gly Gln Glu Thr Glu Ala Arg lle Ser Leu Glu Ala Leu<br>50 55 60  |
| Lys Ala Asp Ala Val Ala Arg Leu Val Ala Arg Gln Trp Ala Gly Val<br>65 70 75 80   |
| Asp Ser Thr Glu Asp Pro Glu Glu Pro Pro Asp Val Ser Trp Ala Val<br>85 90 95  |
| Ala Arg Leu Tyr His Leu Leu Ala Glu Glu Lys Leu Cys Pro Ala Ser<br>100 105 110   |
|  |
| Leu Arg Asp Val Ala Tyr Gln Glu Ala Val Arg Thr Leu Ser Ser Arg<br>115 120 125   |

| G y<br>145                      | Trp                             | Asp                                    | He  | Ala                                    | 150                      | Asp                             | Pro                             | Gly                                    | Ser                         | 11e<br>155                      | Arg                             | Thr                             | L   | Gln                             | Ser<br>160                      |
|---------------------------------|---------------------------------|--|---|--|--------------------------|---------------------------------|---------------------------------|--|-----------------------------|---------------------------------|---------------------------------|---------------------------------|---|---------------------------------|---------------------------------|
| Asn                             | Leu                             | Gly                                    | Cys   | Leu<br>165                             | Pro                      | Pro                             | Ser                             | Ser                                    | Ala<br>170                  | Leu                             | Pro                             | Ser                             | Gly   | Thr<br>175                      | Arg                             |
| Ser                             | Leu                             | Pro                                    | Arg<br>180                                    | Pro                                    | Пe                       | Asp                             | Gly                             | Va I<br>185                            | Ser                         | Asp                             | Trp                             | Ser                             | GIn<br>190                                    | Gly                             | Cys                             |
| Ser                             | Leu                             | Arg<br>195                             | Ser   | Thr                                    | Gly                      | Ser                             | Pro<br>200                      | Ala                                    | Ser                         | Leu                             | Ala                             | Ser<br>205                      | Asn   | Leu                             | Glu                             |
| lle                             | Ser<br>210                      | Gln                                    | Ser   | Pro                                    | Thr                      | Met<br>215                      | Pro                             | Phe                                    | Leu                         | Ser                             | Leu<br>220                      | His                             | Arg   | Ser                             | Pro                             |
| His<br>225                      | Gly                             | Pro                                    | Ser   | Lys                                    | Leu<br>230               | Cys                             | Asp                             | Asp                                    | Pro                         | GIn<br>235                      | Ala                             | Ser                             | Leu   | Val                             | Pro<br>240                      |
| Glu                             | Pro                             | Val                                    | Pro   | Gly<br>245                             | Gly                      | Cys                             | Gln                             | Glu                                    | Pro<br>250                  | Glu                             | Glu                             | Met                             | Ser   | Trp<br>255                      | Pro                             |
| Pro                             | Ser                             | Gly                                    | Glu<br>260                                    | He                                     | Ala                      | Ser                             | Pro                             | Pro<br>265                             | Glu                         | Leu                             | Pro                             | Ser                             | Ser<br>270                                    | Pro                             | Pro                             |
| Pro                             | Gly                             | Leu<br>275                             | Pro   | Glu                                    | Val                      | Ala                             | Pro<br>280                      | Asp                                    | Ala                         | Thr                             | Ser                             | Thr<br>285                      | Gly   | Leu                             | Pro                             |
| Asp                             | Thr<br>290                      | Pro                                    | Ala   | Ala                                    | Pro                      | Glu<br>295                      | Thr                             | Ser                                    | Thr                         | Asn                             | Tyr<br>300                      | Pro                             | Val   | Glu                             | Cys                             |
| Thr<br>305                      | Glu                             | Gly                                    | Ser   | Ala                                    | Gly<br>310               | Pro                             | Gln                             | Ser                                    | Leu                         | Pro<br>315                      | Leu                             | Pro                             | He  | Leu                             | Glu<br>320                      |
| Pro                             | Val                             | Lys                                    | Asn   | Pro<br>325                             | Cys                      | Ser                             | Val                             | Lys                                    |                             | Gln                             | Thr                             | Pro                             | Leu   | GIn<br>335                      | Leu                             |
|                                 |                                 |  |   |  |                          |                                 |                                 |  | 330                         |                                 |                                 |                                 |   | 333                             |                                 |
| Ser                             | Val                             | Glu                                    | Asp<br>340                                    | Thr                                    | Thr                      | Ser                             | Pro                             | Asn<br>345                             |                             | Lys                             | Pro                             | Cys                             | Pro<br>350                                    | Pro                             | Thr                             |
|                                 |                                 |  | 340   |  |                          |                                 |                                 | 345                                    | Thr                         |                                 |                                 |                                 | 350   |                                 |                                 |
| Pro                             | Thr                             | Thr<br>355                             | 340<br>Pro                                    | Głu                                    | Thr                      | Ser                             | Pro<br>360                      | 345<br>Pro                             | Thr<br>Pro                  | Pro                             | Pro                             | Pro<br>365                      | 350<br>Pro                                    | Pro                             | Ser                             |
| Pro<br>Ser                      | Thr<br>Thr<br>370               | Thr<br>355<br>Pro                      | 340<br>Pro<br>Cys                             | Głu<br>Ser                             | Thr<br>Ala               | Ser<br>His<br>375               | Pro<br>360<br>Leu               | 345<br>Pro<br>Thr                      | Thr<br>Pro<br>Pro           | Pro<br>Ser                      | Pro<br>Ser<br>380               | Pro<br>365<br>Leu               | 350<br>Pro<br>Phe                             | Pro<br>Pro                      | Ser<br>Ser                      |
| Pro<br>Ser<br>Ser<br>385        | Thr<br>Thr<br>370<br>Leu        | Thr<br>355<br>Pro<br>Glu               | 340<br>Pro<br>Cys<br>Ser                      | Glu<br>Ser<br>Ser                      | Thr<br>Ala<br>Ser<br>390 | Ser<br>His<br>375<br>Glu        | Pro<br>360<br>Leu<br>GIn        | 345<br>Pro<br>Thr<br>Lys               | Thr<br>Pro<br>Pro<br>Phe    | Pro<br>Ser<br>Tyr<br>395        | Pro<br>Ser<br>380<br>Asn        | Pro<br>365<br>Leu<br>Phe        | 350<br>Pro<br>Phe<br>Val                      | Pro<br>Pro<br>Pro               | Ser<br>Ser<br>Leu<br>400        |
| Pro<br>Ser<br>Ser<br>385<br>His | Thr<br>Thr<br>370<br>Leu<br>Ala | Thr<br>355<br>Pro<br>Glu<br>Arg        | 340<br>Pro<br>Cys<br>Ser<br>Ala               | Głu<br>Ser<br>Ser<br>Asp<br>405        | Thr Ala Ser 390 Glu      | Ser<br>His<br>375<br>Glu<br>His | Pro<br>360<br>Leu<br>GIn        | 345<br>Pro<br>Thr<br>Lys               | Thr Pro Pro Phe Leu 410     | Pro<br>Ser<br>Tyr<br>395<br>Arg | Pro<br>Ser<br>380<br>Asn<br>Val | Pro<br>365<br>Leu<br>Phe        | 350<br>Pro<br>Phe<br>Val<br>Glu               | Pro Pro Ile                     | Ser<br>Ser<br>Leu<br>400<br>Leu |
| Pro<br>Ser<br>Ser<br>385<br>His | Thr<br>370<br>Leu<br>Ala        | Thr<br>355<br>Pro<br>Glu<br>Arg<br>Leu | 340<br>Pro<br>Cys<br>Ser<br>Ala<br>Gly<br>420 | Glu<br>Ser<br>Ser<br>Asp<br>405<br>Val | Thr Ala Ser 390 Glu Pro  | Ser His 375 Glu His             | Pro<br>360<br>Leu<br>GIn<br>IIe | 345<br>Pro<br>Thr<br>Lys<br>Ala<br>425 | Thr Pro Pro Phe Leu 410 Thr | Pro<br>Ser<br>Tyr<br>395<br>Arg | Pro<br>Ser<br>380<br>Asn<br>Val | Pro<br>365<br>Leu<br>Phe<br>Arg | 350<br>Pro<br>Phe<br>Val<br>Glu<br>Asp<br>430 | Pro<br>Pro<br>Ile<br>Lys<br>415 | Ser  Ser  Leu 400  Leu GIn      |



Ser Leu His Gln Val Asn Gln Ala Met Met Ser Asn Leu Thr Arg Gln 465 470 475 480

Gly Ser Pro Asp Cys Val IIe Pro Phe Leu Pro Leu Glu Ser Ser Pro 485 490 495

Ala Gl<br/>n Leu Ser Ser Asp Thr Ala Ser Leu Leu Ser Gly Leu Val Arg<br/> 500 505 510

Leu Asp Glu His Ser Gln lle Phe Ala Arg Lys Val Ala Asn Thr Phe 515 520 525

Lys Pro His Arg Leu Gln Ala Arg Lys Ala Met Trp Arg Lys Glu Gln 530 540

Asp Thr Arg Ala Leu Arg Glu Gln Ser Gln His Leu Asp Gly Glu Arg 545 550 555 560

Met Gln Ala Ala Ala Leu Asn Ala Ala Tyr Ser Ala Tyr Leu Gln Ser 565 570 575

Tyr Leu Ser Tyr Gln Ala Gln Met Glu Gln Leu Gln Val Ala Phe Gly 580 585 590

Ser His Met Ser Phe Gly Thr Gly Ala Pro Tyr Gly Ala Arg Met Pro 595 600 605

Phe Gly Gly Gln Val Pro Leu Gly Ala Pro Pro Pro Phe Pro Thr Trp 610 620

Pro Gly Cys Pro Gln Pro Pro Pro Leu His Ala Trp Gln Ala Gly Thr 625 630 635 640

Pro Pro Pro Pro Ser Pro Gln Pro Ala Ala Phe Pro Gln Ser Leu Pro 645 650 655

Phe Pro Gln Ser Pro Ala Phe Pro Thr Ala Ser Pro Ala Pro Pro Gln 660 665 670

Ser Pro Gly Leu Gln Pro Leu IIe IIe His His Ala Gln Met Val Gln 675 680 685

Leu Gly Leu Asn Asn His Met Trp Asn Gln Arg Gly Ser Gln Ala Pro 690 695 700

Glu Asp Lys Thr Gln Glu Ala Glu 705 710

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Thr Ser Ala Phe Gly Arg Glu Val Asp Lys Met Glu Gln Leu Glu Gly



|  |  |     | ctc<br>Leu        |     |     |     |     |     |     |  | 871  |
|--|--|-----|-------------------|-----|-----|-----|-----|-----|-----|--|------|
|  |  |     | tcc<br>Ser        |     |     |     |     |     |     |  | 919  |
|  |  |     | ctg<br>Leu<br>220 |     |     |     |     |     |     |  | 967  |
|  |  |     | ctg<br>Leu        |     |     |     |     |     |     |  | 1015 |
|  |  |     | cac<br>His        |     |     |     |     |     |     |  | 1063 |
|  |  |     | ttc<br>Phe        |     |     |     |     |     |     |  | 1111 |
|  |  |     | gtg<br>Val        |     |     |     |     |     |     |  | 1159 |
|  |  |     | cac<br>His<br>300 |     |     |     |     |     |     |  | 1207 |
|  |  |     | cgg<br>Arg        |     |     |     |     |     |     |  | 1255 |
|  |  | Phe | aag<br>Lys        | Met | Phe | Gly | Ser | Phe | Lys |  | 1303 |
|  |  |     | gag<br>Glu        |     |     |     |     |     |     |  | 1351 |
|  |  |     | ctc<br>Leu        |     |     |     |     |     |     |  | 1399 |
|  |  |     | agg<br>Arg<br>380 |     |     |     |     |     |     |  | 1447 |
|  |  |     | aag<br>Lys        |     |     |     |     |     |     |  | 1495 |

| agg<br>Arg        | aag<br>Lys | acc<br>Thr        | gag<br>Glu        | gag<br>Glu<br>410 | g<br>Pro          | cgc<br>Arg        | gcc<br>Ala        | aag<br>Lys        | gag<br>Glu<br>415 | gcc<br>Ala        | gtc<br>Val | gtc<br>Val        | g<br>Ala          | atg<br>Met<br>420 | atc<br>  e        | 1543 |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------------|-------------------|-------------------|-------------------|-------------------|------|
|                   |            |                   |                   |                   |                   | atc<br>lle        |                   |                   |                   |                   |            |                   |                   |                   |                   | 1591 |
| cgg<br>Arg        | cag<br>Gln | gag<br>Glu<br>440 | cgg<br>Arg        | cag<br>Gln        | cgg<br>Arg        | ctg<br>Leu        | gcg<br>Ala<br>445 | gcc<br>Ala        | gtg<br>Val        | gtg<br>Val        | agc<br>Ser | cgc<br>Arg<br>450 | atc<br>Ile        | gac<br>Asp        | gcc<br>Ala        | 1639 |
|                   |            |                   |                   |                   |                   | agc<br>Ser<br>460 |                   |                   |                   |                   |            |                   |                   |                   |                   | 1687 |
| gaa<br>Glu<br>470 | ttt<br>Phe | ctg<br>Leu        | cac<br>His        | ctg<br>Leu        | gac<br>Asp<br>475 | ttg<br>Leu        | aca<br>Thr        | gcg<br>Ala        | ccc<br>Pro        | atc<br>Ile<br>480 | cct<br>Pro | ggc<br>Gly        | gcc<br>Ala        | tcc<br>Ser        | ccg<br>Pro<br>485 | 1735 |
|                   |            |                   |                   |                   |                   | ctg<br>Leu        |                   |                   |                   |                   |            |                   |                   |                   |                   | 1783 |
| ggg<br>G y        | aag<br>Lys | gac<br>Asp        | agc<br>Ser<br>505 | aag<br>Lys        | atg<br>Met        | gat<br>Asp        | gtg<br>Val        | tac<br>Tyr<br>510 | tgc<br>Cys        | ttc<br>Phe        | ctc<br>Leu | ttc<br>Phe        | acg<br>Thr<br>515 | gat<br>Asp        | ctg<br>Leu        | 1831 |
|                   |            |                   |                   |                   |                   | gtg<br>Val        |                   |                   |                   |                   |            |                   |                   |                   |                   | 1879 |
|                   |            |                   |                   |                   |                   | gac<br>Asp<br>540 |                   |                   |                   |                   |            |                   |                   |                   |                   | 1927 |
|                   | Gly        | Ser               | Phe               | Leu               | Leu               | atc<br>He         | Tyr               | Leu               | Asn               | Glu               | Phe        | His               | Ser               | Ala               |                   | 1975 |
| ggg<br>Gly        | gcc<br>Ala | tac<br>Tyr        | acg<br>Thr        | ttc<br>Phe<br>570 | cag<br>Gln        | gcc<br>Ala        | agt<br>Ser        | ggc<br>Gly        | cag<br>Gln<br>575 | gcc<br>Ala        | ttg<br>Leu | tgc<br>Cys        | cgt<br>Arg        | ggc<br>Gly<br>580 | tgg<br>Trp        | 2023 |
| gtg<br>Val        | gac<br>Asp | acc<br>Thr        | att<br>  e<br>585 | tac<br>Tyr        | aat<br>Asn        | gcc<br>Ala        | cag<br>Gln        | aac<br>Asn<br>590 | cag<br>Gln        | ctg<br>Leu        | caa<br>Gln | cag<br>Gln        | ctg<br>Leu<br>595 | cgt<br>Arg        | gca<br>Ala        | 2071 |
|                   |            |                   |                   |                   |                   | cag<br>Gln<br>′   |                   |                   |                   |                   |            |                   |                   |                   |                   | 2119 |
|                   |            |                   |                   |                   |                   | gaa<br>Glu<br>620 |                   |                   |                   |                   |            |                   |                   |                   |                   | 2167 |
|                   |            |                   |                   |                   |                   | tca<br>Ser        |                   |                   |                   |                   |            |                   |                   |                   |                   | 2215 |

gcc cct agc cct ggc agc ggt cct ggg cta gtc ggc tgc ctg gcc ggg Ala Pro Ser Pro Gly Ser Gly Pro Gly Leu Val Gly Cys Leu Ala Gly

gaa cct gca ggc tcc cac agg aag agg tgt gga gac ctg ccc tcg ggg Glu Pro Ala Gly Ser His Arg Lys Arg Cys Gly Asp Leu Pro Ser Gly

gcc tct ccc agg gto ag cct gag ccc cca cca ggg gtc to gcc cag 2935 Ala Ser Pro Arg Val Gln Pro Glu Pro Pro Pro Gly Val Ser Ala Gln 870 880 885

cac agg aag ctg acc ctg gcc cag ctc tac cga atc agg acc acc ctg 2983 His Arg Lys Leu Thr Leu Ala Gln Leu Tyr Arg lle Arg Thr Thr Leu 890 895 900

ctg ctt aac tcc acg ctc act gcc tcg gag gtc tgagcagagg gaggccccca 3036 Leu Leu Asn Ser Thr Leu Thr Ala Ser Glu Val 905 910

agagtgccat tgaccaagag acagcagaca gcctgcctcc tggggcgtgc cggcacctgc 3096 ttcagctact gcctcctgta tgcatgagcc ggatgctggg caggatccct gcctacgccc 3156 gggcccgatt tgcgctttgc cggactggat ggagtggagg aggcccaggc cacagtacca 3216 ccccacctgc ccaggcagcc cctcgtcacc tactccccga agttaccagc tcagctcgag 3276 tcttcagggc tgggctccta ggctgcccat cctacttcta ccctcactgg cctccagtgg 3336 gattcactcc tgccctgccc ccaccttccc agtcccacag gccacccctg gcttgggctg 3396 ggttctgtga agttacgtat ttattgagct tttggttctt ttataaagac ttgtctagac 3456

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Lys Gly lle Ala Leu Gly Lys Val Asp lle Tyr Leu Asp Gln Ser Asn 20 25 30

Thr Pro Leu Ser Leu Thr Phe Glu Ala Tyr Arg Phe Gly Gly His Tyr 35 40 45

Leu Arg Val Lys Ala Pro Ala Lys Pro Gly Asp Glu Gly Lys Val Glu 50 55 60

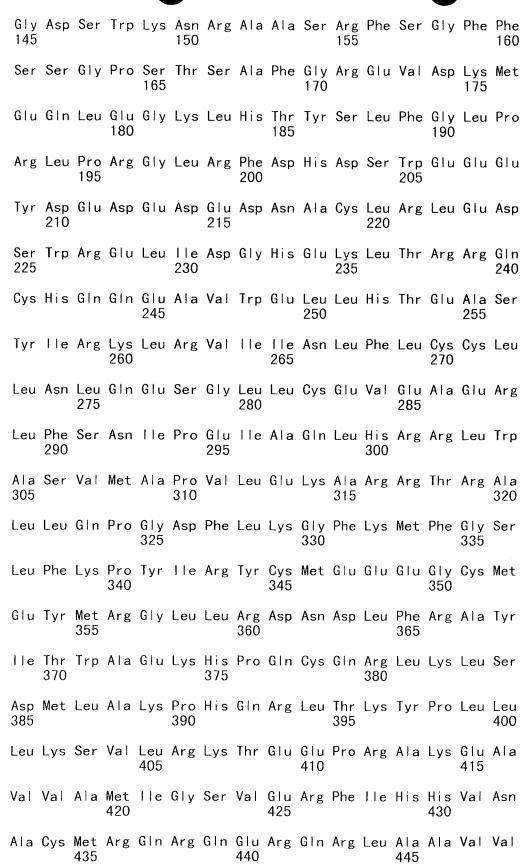
Gln Gly Met Lys Asp Ser Lys Ser Leu Ser Leu Pro IIe Leu Arg Pro 65 70 75 80

Ala Gly Thr Gly Pro Pro Ala Leu Glu Arg Val Asp Ala Gln Ser Arg 85 90 95

Arg Glu Ser Leu Asp IIe Leu Ala Pro Gly Arg Arg Arg Lys Asn Met 100 105 110

Ser Glu Phe Leu Gly Glu Ala Ser lle Pro Gly Gln Glu Pro Pro Thr 115 120 125

Pro Ser Ser Cys Ser Leu Pro Ser Gly Ser Ser Gly Ser Thr Asn Thr



Ser Arg Ile Asp Ala Tyr Glu Val Val Glu Ser Ser Ser Asp Glu Val Asp Lys Leu Leu Lys Glu Phe Leu His Leu Asp Leu Thr Ala Pro Ile Pro Gly Ala Ser Pro Glu Glu Thr Arg Gln Leu Leu Glu Gly Ser 490 Leu Arg Met Lys Glu Gly Lys Asp Ser Lys Met Asp Val Tyr Cys Phe 505 Leu Phe Thr Asp Leu Leu Leu Val Thr Lys Ala Val Lys Lys Ala Glu Arg Thr Arg Val IIe Arg Pro Pro Leu Leu Val Asp Lys IIe Val Cys Arg Glu Leu Arg Asp Pro Gly Ser Phe Leu Leu Ile Tyr Leu Asn Glu Phe His Ser Ala Val Gly Ala Tyr Thr Phe Gln Ala Ser Gly Gln Ala Leu Cys Arg Gly Trp Val Asp Thr lle Tyr Asn Ala Gln Asn Gln Leu Gln Gln Leu Arg Ala Gln Glu Pro Pro Gly Ser Gln Gln Pro Leu Gln Ser Leu Glu Glu Glu Glu Asp Glu Gln Glu Glu Glu Glu Glu Glu Glu 610 Glu Glu Glu Glu Gly Glu Asp Ser Gly Thr Ser Ala Ala Ser Ser Pro Thr lle Met Arg Lys Ser Ser Gly Ser Pro Asp Ser Gln His Cys Ala Ser Asp Gly Ser Thr Glu Thr Leu Ala Met Val Val Glu Pro Gly Asp Thr Leu Ser Ser Pro Glu Phe Asp Ser Gly Pro Phe Ser Ser Gln Ser Asp Glu Thr Ser Leu Ser Thr Thr Ala Ser Ser Ala Thr Pro 695 Thr Ser Glu Leu Leu Pro Leu Gly Pro Val Asp Gly Arg Ser Cys Ser 705 Met Asp Ser Ala Tyr Gly Thr Leu Ser Pro Thr Ser Leu Gln Asp Phe Val Ala Pro Gly Pro Met Ala Glu Leu Val Pro Arg Ala Pro Glu Ser

|  |                    |                                  |            | 4          |            |            |                    |            |              |            | •            |                  | -          |            |            |     |
|--|--------------------|----------------------------------|------------|------------|------------|------------|--------------------|------------|--------------|------------|--------------|------------------|------------|------------|------------|-----|
| Pro  | Arg                | Val<br>755                       | Pro        | Se         | •          | Pro        | Pro<br>760         | Ser        | Pro          | Arg        | Leu          | Arg<br>765       |            | Arg        | Thr        |     |
| Pro  | Va l<br>770        | Gin                              | Leu        | Leu        | Ser        | Cys<br>775 | Pro                | Pro        | His          | Leu        | Leu<br>780   | Lys              | Ser        | Lys        | Ser        |     |
| Glu<br>785                                   | Ala                | Ser                              | Leu        | Leu        | GIn<br>790 | Leu        | Leu                | Ala        | Gly          | Ala<br>795 | Gly          | Thr              | His        | Gly        | Thr<br>800 |     |
| Pro  | Ser                | Ala                              | Pro        | Ser<br>805 | Arg        | Ser        | Leu                | Ser        | G I u<br>810 | Leu        | Cys          | Leu              | Ala        | Val<br>815 | Pro        |     |
| Ala  | Pro                | Gly                              | 11e<br>820 | Arg        | Thr        | Gln        | Gly                | Ser<br>825 | Pro          | Gln        | Glu          | Ala              | Gly<br>830 | Pro        | Ser        |     |
| Trp  | Asp                | Cys<br>835                       | Arg        | Gly        | Ala        | Pro        | Ser<br>840         | Pro        | Gly          | Ser        | Gly          | Pro<br>845       | Gly        | Leu        | Val        |     |
| Gly  | Cys<br>850         | Leu                              | Ala        | Gly        | Glu        | Pro<br>855 | Ala                | Gly        | Ser          | His        | Arg<br>860   | Lys              | Arg        | Cys        | Gly        |     |
| Asp<br>865                                   | Leu                | Pro                              | Ser        | Gly        | Ala<br>870 | Ser        | Pro                | Arg        | Val          | GIn<br>875 | Pro          | Glu              | Pro        | Pro        | Pro<br>880 |     |
| Gly  | Val                | Ser                              | Ala        | GIn<br>885 | His        | Arg        | Lys                | Leu        | Thr<br>890   | Leu        | Ala          | Gln              | Leu        | Tyr<br>895 | Arg        |     |
| lle  | Arg                | Thr                              | Thr<br>900 | Leu        | Leu        | Leu        | Asn                | Ser<br>905 | Thr          | Leu        | Thr          | Ala              | Ser<br>910 | Glu        | Val        |     |
| <211<br><212<br><213<br><220<br><221<br><222 | > CD<br>!> (1      | 609<br>IA<br>Imo s<br>IS<br>52). |            |            |            |            |                    |            |              |            |              |                  |            |            |            |     |
|  | )> 15<br>.gaag     |                                  | aggg       | agag       | g aa       | aggg       | tgga               | cct        | gagg         | ccc        | ccat         | ggag             | aa g       | ggac       | gggca      | 60  |
| ggat   | gtat               | gt c                             | асса       | cgcc       | g ac       | tgcc       | agca               | gct        | gcac         | cgc        | cggg         | ggcc             | cc t       | caac       | ctctg      | 120 |
| cgag   | gcct               | gt g                             | acag       | caag       | t tc       | caca       | gcac               |            |              |            | at g<br>yr A |                  |            |            |            | 172 |
| cgc<br>Arg                                   | ttc<br>Phe         | gac<br>Asp<br>10                 | ctt<br>Leu | ccc<br>Pro | cca<br>Pro | caa<br>Gln | ggc<br>Gly :<br>15 | tct<br>Ser | gtg<br>Val   | ctg<br>Leu | gcc<br>Ala   | cgg<br>Arg<br>20 | aac<br>Asn | gtg<br>Val | tcc<br>Ser | 220 |
|  | cgg<br>Arg 3<br>25 |                                  |            |            |            |            |                    |            |              |            |              |                  |            |            |            | 268 |

| gag<br>Glu<br>40  | gag<br>Glu        | gag<br>Glu        | gag<br>Glu        | agc<br>Ser        | Ser<br>45         | gtg<br><b>Va</b> l | gat<br>Asp        | ggc<br>Gly        | aaa<br>Lys        | ggg<br>Gly<br>50  | gac<br>Asp        | cgg<br>Arg        | aag<br>Lys        | agc<br>Ser        | aca<br>Thr<br>55  | 316 |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|--------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-----|
| ggc<br>Gly        | ctg<br>Leu        | aaa<br>Lys        | ctc<br>Leu        | tcc<br>Ser<br>60  | aag<br>Lys        | aag<br>Lys         | aaa<br>Lys        | gca<br>Ala        | agg<br>Arg<br>65  | agg<br>Arg        | aga<br>Arg        | cac<br>His        | acg<br>Thr        | gat<br>Asp<br>70  | gac<br>Asp        | 364 |
| cca<br>Pro        | agc<br>Ser        | aag<br>Lys        | gaa<br>Glu<br>75  | tgc<br>Cys        | ttc<br>Phe        | act<br>Thr         | ctg<br>Leu        | aaa<br>Lys<br>80  | ttt<br>Phe        | gac<br>Asp        | ctg<br>Leu        | aat<br>Asn        | gtg<br>Val<br>85  | gac<br>Asp        | att<br>lle        | 412 |
| gag<br>Glu        | aca<br>Thr        | gag<br>Glu<br>90  | atc<br>Ile        | gtc<br>Val        | cca<br>Pro        | gcc<br>Ala         | atg<br>Met<br>95  | aag<br>Lys        | aag<br>Lys        | aag<br>Lys        | tca<br>Ser        | ctg<br>Leu<br>100 | ggg<br>Gly        | gag<br>Glu        | gtg<br>Val        | 460 |
| ctg<br>Leu        | ctg<br>Leu<br>105 | cct<br>Pro        | gta<br>Val        | ttt<br>Phe        | gaa<br>Glu        | agg<br>Arg<br>110  | aag<br>Lys        | ggc<br>Gly        | att<br>lle        | gcg<br>Ala        | ctg<br>Leu<br>115 | ggc<br>Gly        | aaa<br>Lys        | gtg<br>Val        | gac<br>Asp        | 508 |
| atc<br>lle<br>120 | tac<br>Tyr        | ctg<br>Leu        | gac<br>Asp        | cag<br>Gln        | tcc<br>Ser<br>125 | aac<br>Asn         | aca<br>Thr        | ccc<br>Pro        | ctg<br>Leu        | tcc<br>Ser<br>130 | ctc<br>Leu        | acc<br>Thr        | ttc<br>Phe        | gag<br>Glu        | gcc<br>Ala<br>135 | 556 |
| tac<br>Tyr        | agg<br>Arg        | ttc<br>Phe        | ggg<br>Gly        | gga<br>Gly<br>140 | cac<br>His        | tac<br>Tyr         | ctt<br>Leu        | cgt<br>Arg        | gtc<br>Val<br>145 | aaa<br>Lys        | gcc<br>Ala        | cca<br>Pro        | gcc<br>Ala        | aag<br>Lys<br>150 | cct<br>Pro        | 604 |
| gga<br>Gly        | gat<br>Asp        | gag<br>Glu        | ggc<br>Gly<br>155 | aag<br>Lys        | gtg<br>Val        | gag<br>Glu         | cag<br>Gln        | ggc<br>Gly<br>160 | atg<br>Met        | aag<br>Lys        | gac<br>Asp        | tcc<br>Ser        | aag<br>Lys<br>165 | tcc<br>Ser        | ctg<br>Leu        | 652 |
| agt<br>Ser        | ttg<br>Leu        | ccg<br>Pro<br>170 | att<br>Ile        | ctg<br>Leu        | cgg<br>Arg        | cca<br>Pro         | gct<br>Ala<br>175 | ggg<br>Gly        | acc<br>Thr        | ggg<br>Gly        | ccc<br>Pro        | ccc<br>Pro<br>180 | gcc<br>Ala        | ctg<br>Leu        | gag<br>Glu        | 700 |
| cgt<br>Arg        | gtg<br>Val<br>185 | gac<br>Asp        | gcc<br>Ala        | cag<br>G n        | agc<br>Ser        | cgc<br>Arg<br>190  | cgg<br>Arg        | gag<br>Glu        | agc<br>Ser        | ctg<br>Leu        | gac<br>Asp<br>195 | atc<br>Ile        | ttg<br>Leu        | gcc<br>Ala        | cct<br>Pro        | 748 |
| ggc<br>Gly<br>200 | Arg               | cgc<br>Arg        | cgc<br>Arg        | aag<br>Lys        | aac<br>Asn<br>205 | atg<br>Met         | tcg<br>Ser        | gag<br>Glu        | ttc<br>Phe        | ctg<br>Leu<br>210 | Gly               | gag<br>Glu        | gcg<br>Ala        | agc<br>Ser        | atc<br>lle<br>215 | 796 |
| ccc<br>Pro        | ggg<br>Gly        | cag<br>Gln        | gag<br>Glu        | ccc<br>Pro<br>220 | Pro               | acg<br>Thr         | ccc<br>Pro        | tcc<br>Ser        | agc<br>Ser<br>225 | Cys               | tct<br>Ser        | ctg<br>Leu        | ccc<br>Pro        | agc<br>Ser<br>230 | Gly               | 844 |
| agc<br>Ser        | agt<br>Ser        | ggc<br>Gly        | agc<br>Ser<br>235 | Thr               | aac<br>Asn        | act<br>Thr         | ggc<br>Gly        | gac<br>Asp<br>240 | Ser               | tgg<br>Trp        | aag<br>Lys        | aac<br>Asn        | cgg<br>Arg<br>245 | Ala               | gcc<br>Ala        | 892 |
| agt<br>Ser        | cgc<br>Arg        | ttc<br>Phe<br>250 | Ser               | ggc<br>Gly        | ttt<br>Phe        | ttc<br>Phe         | ago<br>Ser<br>255 | Ser               | ggc<br>Gly        | ccc<br>Pro        | ago<br>Ser        | acc<br>Thr<br>260 | Ser               | gcc<br>Ala        | ttt<br>Phe        | 940 |
| ggc<br>Gly        | cgg<br>Arg        | gag<br>Glu        | gta<br>Val        | gac<br>Asp        | aag<br>Lys        | atg<br>Met         | gag               | cag<br>Gln        | ctg<br>Leu        | gag               | ggc<br>Gly        | aag<br>Lys        | ctg<br>Leu        | cac<br>His        | acc<br>Thr        | 988 |

| tac<br>Tyr<br>280 | Ser               | cto<br>Leu        | tto<br>Phe        | gge<br>Gly          | ctg<br>Leu<br>285 | Pro               | agg<br>Arg        | g ctg<br>g Leu    | ccc<br>Pro        | cgg<br>Arg<br>290 | 5 Gly             | g ctg<br>/ Leu    | g cgc<br>ı Arg    | tto<br>Phe        | gac<br>Asp<br>295 | 1036 |
|-------------------|-------------------|-------------------|-------------------|---------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| cat<br>His        | gac<br>Asp        | tcc<br>Ser        | tgg<br>Trp        | g gag<br>Glu<br>300 | ı Glu             | gag<br>Glu        | g tac<br>ı Tyr    | gat<br>Asp        | gaa<br>Glu<br>305 | ı Asp             | gag<br>Glu        | g gat<br>ı Asp    | gag<br>Glu        | gac<br>Asp<br>310 | aat<br>Asn        | 1084 |
| gcc<br>Ala        | tgo<br>Cys        | ctg<br>Leu        | agg<br>Arg<br>315 | Leu                 | gag<br>Glu        | gac<br>Asp        | ago<br>Ser        | tgg<br>Trp<br>320 | Arg               | gag<br>Glu        | cto<br>Leu        | att<br>Ille       | gat<br>Asp<br>325 | Gly               | cat<br>His        | 1132 |
| gag<br>Glu        | aag<br>Lys        | ctg<br>Leu<br>330 | lhr               | cgg<br>Arg          | cgg<br>Arg        | cag<br>G n        | tgc<br>Cys<br>335 | His               | cag<br>G n        | cag<br>G n        | gag<br>Glu        | gcg<br>Ala<br>340 | Val               | tgg<br>Trp        | gag<br>Glu        | 1180 |
| ctg<br>Leu        | ctg<br>Leu<br>345 | HIS               | acg<br>Thr        | gag<br>Glu          | gcc<br>Ala        | tcc<br>Ser<br>350 | Tyr               | atc<br>lle        | agg<br>Arg        | aaa<br>Lys        | ctg<br>Leu<br>355 | cgg<br>Arg        | gtg<br>Val        | atc<br>lle        | atc<br>lle        | 1228 |
| aac<br>Asn<br>360 | ctg<br>Leu        | ttc<br>Phe        | ctg<br>Leu        | tgc<br>Cys          | tgc<br>Cys<br>365 | ctc<br>Leu        | ctg<br>Leu        | aac<br>Asn        | ctg<br>Leu        | caa<br>Gln<br>370 | gag<br>Glu        | tca<br>Ser        | ggg<br>Gly        | ctg<br>Leu        | ctg<br>Leu<br>375 | 1276 |
| tgt<br>Cys        | gag<br>Glu        | gtg<br>Val        | gag<br>G u        | gcg<br>Ala<br>380   | gag<br>Glu        | cgc<br>Arg        | ctg<br>Leu        | ttc<br>Phe        | agc<br>Ser<br>385 | aac<br>Asn        | atc<br>lle        | ccg<br>Pro        | gag<br>Glu        | atc<br>  e<br>390 | gcg<br>Ala        | 1324 |
| cag<br>Gln        | ctg<br>Leu        | cac<br>His        | cgc<br>Arg<br>395 | agg<br>Arg          | ctg<br>Leu        | tgg<br>Trp        | gct<br>Ala        | agc<br>Ser<br>400 | gtg<br>Val        | atg<br>Met        | gcg<br>Ala        | ccg<br>Pro        | gtg<br>Val<br>405 | ctg<br>Leu        | gag<br>Glu        | 1372 |
| aag<br>Lys        | gcg<br>Ala        | cgg<br>Arg<br>410 | cgc<br>Arg        | acg<br>Thr          | cga<br>Arg        | gcg<br>Ala        | ctg<br>Leu<br>415 | cta<br>Leu        | cag<br>G n        | ccc<br>Pro        | ggg<br>Gly        | gac<br>Asp<br>420 | ttc<br>Phe        | ctc<br>Leu        | aaa<br>Lys        | 1420 |
| Gly               | ttc<br>Phe<br>425 | aag<br>Lys        | atg<br>Met        | ttc<br>Phe          | ggc<br>Gly        | tcg<br>Ser<br>430 | ctc<br>Leu        | ttc<br>Phe        | aag<br>Lys        | ccc<br>Pro        | tac<br>Tyr<br>435 | atc<br>lle        | cgc<br>Arg        | tac<br>Tyr        | tgc<br>Cys        | 1468 |
| atg<br>Met<br>440 | gag<br>Glu        | gag<br>Glu        | gag<br>G u        | ggc<br>Gly          | tgc<br>Cys<br>445 | atg<br>Met        | gag<br>Glu        | tac<br>Tyr        | atg<br>Met        | cgc<br>Arg<br>450 | ggc<br>Gly        | ctg<br>Leu        | ctg<br>Leu        | cgc<br>Arg        | gac<br>Asp<br>455 | 1516 |
| aac<br>Asn        | gac<br>Asp        | ctc<br>Leu        | ttc<br>Phe        | cgg<br>Arg<br>460   | gcc<br>Ala        | tac<br>Tyr        | atc<br>lle        | Thr               | tgg<br>Trp<br>465 | gcg<br>Ala        | gag<br>Glu        | aag<br>Lys        | His               | cca<br>Pro<br>470 | cag<br>Gln        | 1564 |
| tgc<br>Cys        | cag<br>G n        | Arg               | ctg<br>Leu<br>475 | aag<br>Lys          | ctg<br>Leu        | agc<br>Ser        | Asp               | atg<br>Met<br>480 | ctg<br>Leu        | gcc<br>Ala        | aaa<br>Lys        | Pro               | cac<br>His<br>485 | cag<br>Gln        | cgg<br>Arg        | 1612 |
| ctc a             | Ihr               | aag<br>Lys<br>490 | tac<br>Tyr        | ccg<br>Pro          | ctg<br>Leu        | Leu               | ctc<br>Leu<br>495 | aag<br>Lys        | tcg<br>Ser        | gtg<br>Val        | Leu               | agg<br>Arg<br>500 | aag<br>Lys        | acc<br>Thr        | gag<br>Glu        | 1660 |

| gag<br>Glu        | ccg<br>Pro<br>505 | Arg        | gcc<br>Ala | aag<br>Lys | g<br>Glu          | gcc<br>Ala<br>510 | gtc<br>Val | gtc<br>Val | gcc<br>Ala | atg<br>Met        | atc<br>  e<br>515 | ggc<br>Gly | t<br>Ser   | gtg<br>Val | gag<br>Glu        | 1708 |
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|                   | ttc<br>Phe        |            |            |            |                   |                   |            |            |            |                   | Gln               |            |            |            |                   | 1756 |
|                   | cgg<br>Arg        |            |            |            |                   |                   |            |            |            | Asp               |                   |            |            |            |                   | 1804 |
|                   | agc<br>Ser        |            |            |            |                   |                   |            |            |            |                   |                   |            |            |            |                   | 1852 |
|                   | gac<br>Asp        |            |            |            |                   |                   |            |            |            |                   |                   |            |            |            |                   | 1900 |
|                   | ctg<br>Leu<br>585 |            |            |            |                   |                   |            |            |            |                   |                   |            |            |            |                   | 1948 |
|                   | atg<br>Met        |            |            |            |                   |                   |            |            |            |                   |                   |            |            |            |                   | 1996 |
|                   | gca<br>Ala        |            |            |            |                   |                   |            |            |            |                   |                   |            |            |            |                   | 2044 |
|                   | gtg<br>Val        |            |            |            |                   |                   |            |            |            |                   |                   |            |            |            |                   | 2092 |
| ctc<br>Leu        | ctt<br>Leu        | Пe         | Tyr        | Leu        | aat<br>Asn        | Glu               | Phe        | His        | Ser        | Ala               | Val               | Gly        | Ala        | tac<br>Tyr | acg<br>Thr        | 2140 |
| ttc<br>Phe        | cag<br>Gln<br>665 | gcc<br>Ala | agt<br>Ser | ggc<br>Gly | cag<br>G¦n        | gcc<br>Ala<br>670 | ttg<br>Leu | tgc<br>Cys | cgt<br>Arg | ggc<br>Gly        | tgg<br>Trp<br>675 | gtg<br>Val | gac<br>Asp | acc<br>Thr | att<br>He         | 2188 |
| tac<br>Tyr<br>680 | aat<br>Asn        | gcc<br>Ala | cag<br>Gln | aac<br>Asn | cag<br>Gin<br>685 | ctg<br>Leu        | caa<br>Gln | cag<br>Gin | ctg<br>Leu | cgt<br>Arg<br>690 | gca<br>Ala        | cag<br>G n | gag<br>Glu | ccc<br>Pro | cca<br>Pro<br>695 | 2236 |
|                   | agt<br>Ser        |            |            |            |                   |                   |            |            |            |                   |                   |            |            |            |                   | 2284 |
|                   | gag<br>Glu        | Glu        |            |            |                   |                   | Glu        |            |            |                   |                   |            |            |            |                   | 2332 |
| ggc<br>Gly        | act<br>Thr        | tca<br>Ser | gct<br>Ala | gcc<br>Ala | agc<br>Ser        | tcc<br>Ser        | cct<br>Pro | acc<br>Thr | atc<br>lle | atg<br>Met        | cgg<br>Arg        | aaa<br>Lys | agc<br>Ser | agc<br>Ser | ggc<br>Gly        | 2380 |

|            |            | 730        |                   |            |            |            | 735        |                   |            |            |            | 740        |                   |            |            |      |
|------------|------------|------------|-------------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|-------------------|------------|------------|------|
| _          |            | -          | tct<br>Ser        | _          |            | _          | _          |                   | _          |            |            | _          | _                 |            |            | 2428 |
|            |            |            | gtg<br>Val        |            |            |            |            |                   |            |            |            |            |                   |            |            | 2476 |
|            |            |            | cct<br>Pro        |            |            |            |            |                   |            |            |            |            |                   |            |            | 2524 |
|            |            |            | tct<br>Ser<br>795 |            |            |            |            |                   |            |            |            |            |                   |            |            | 2572 |
|            |            |            | cgc<br>Arg        |            |            |            |            |                   |            |            |            |            |                   |            |            | 2620 |
|            |            |            | tta<br>Leu        |            |            |            |            |                   |            |            |            |            |                   |            |            | 2668 |
|            |            |            | gcc<br>Ala        |            |            |            |            |                   |            |            |            |            |                   |            |            | 2716 |
|            |            |            | cgc<br>Arg        |            |            |            |            |                   |            |            |            |            |                   |            |            | 2764 |
|            |            |            | aag<br>Lys<br>875 |            |            |            |            |                   |            |            |            |            |                   |            |            | 2812 |
|            |            |            | acc<br>Thr        |            |            |            |            |                   |            |            |            |            |                   |            |            | 2860 |
|            |            |            | ctg<br>Leu        |            |            |            |            |                   |            |            |            |            |                   |            |            | 2908 |
|            |            |            | gct<br>Ala        |            |            |            |            |                   |            |            |            |            |                   |            |            | 2956 |
|            |            |            | cct<br>Pro        |            |            |            |            |                   |            |            |            |            |                   |            |            | 3004 |
| tcc<br>Ser | cac<br>His | agg<br>Arg | aag<br>Lys<br>955 | agg<br>Arg | tgt<br>Cys | gga<br>Gly | gac<br>Asp | ctg<br>Leu<br>960 | ccc<br>Pro | tcg<br>Ser | ggg<br>Gly | gcc<br>Ala | tct<br>Ser<br>965 | ccc<br>Pro | agg<br>Arg | 3052 |

3100 gtc cag cct gag ccc a cca ggg gtc tct gcc cag cac a Val Gln Pro Glu Pro Pro Pro Gly Val Ser Ala Gln His Arg Lys Leu 975 970 acc ctg gcc cag ctc tac cga atc agg acc acc ctg ctg ctt aac tcc 3148 Thr Leu Ala Gln Leu Tyr Arg lle Arg Thr Thr Leu Leu Leu Asn Ser 990 995 985 3199 acg ctc act gcc tcg gag gtc tgagcagagg gaggccccca agagtgccat Thr Leu Thr Ala Ser Glu Val 1000 1005 tgaccaagag acagcagaca gcctgcctcc tggggcgtgc cggcacctgc ttcagctact 3259 gcctcctgta tgcatgagcc ggatgctggg caggatccct gcctacgccc gggcccgatt 3319 tgcgctttgc cggactggat ggagtggagg aggcccaggc cacagtacca ccccacctgc 3379 ccaggcagcc cctcgtcacc tactccccga agttaccagc tcagctcgag tcttcagggc 3439 tgggctccta ggctgcccat cctacttcta ccctcactgg cctccagtgg gattcactcc 3499 tgccctgccc ccaccttccc agtcccacag gccacccctg gcttgggctg ggttctgtga 3559 3609 agttacgtat ttattgagct tttggttctt ttataaagac ttgtctagac

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Pro Ala Val Asp Leu Glu Glu Glu Glu Glu Glu Glu Ser Ser Val Asp Gly 35 40 45

Lys Gly Asp Arg Lys Ser Thr Gly Leu Lys Leu Ser Lys Lys Ala 50 55 60

Arg Arg Arg His Thr Asp Asp Pro Ser Lys Glu Cys Phe Thr Leu Lys 65 70 75 80

Phe Asp Leu Asn Val Asp lie Glu Thr Glu lie Val Pro Ala Met Lys 85 90 95

Lys Lys Ser Leu Gly Glu Val Leu Leu Pro Val Phe Glu Arg Lys Gly 100 105 110

lle Ala Leu Gly Lys Val Asp Ile Tyr Leu Asp Gln Ser Asn Thr Pro 115 120 125

Leu Ser Leu Thr Phe Glu Ala Tyr Arg Phe Gly Gly His Tyr Leu Arg



Val Lys Ala Pro Ala Lys Pro Gly Asp Glu Gly Lys Val Glu Gln Gly 145 150 155 160

Met Lys Asp Ser Lys Ser Leu Ser Leu Pro IIe Leu Arg Pro Ala Gly 165 170 175

Thr Gly Pro Pro Ala Leu Glu Arg Val Asp Ala Gln Ser Arg Arg Glu 180 185 190

Ser Leu Asp IIe Leu Ala Pro Gly Arg Arg Arg Lys Asn Met Ser Glu 195 200 205

Phe Leu Gly Glu Ala Ser Ile Pro Gly Gln Glu Pro Pro Thr Pro Ser 210 215 220

Ser Cys Ser Leu Pro Ser Gly Ser Ser Gly Ser Thr Asn Thr Gly Asp 225 230 235 240

Ser Trp Lys Asn Arg Ala Ala Ser Arg Phe Ser Gly Phe Phe Ser Ser 245 250 255

Gly Pro Ser Thr Ser Ala Phe Gly Arg Glu Val Asp Lys Met Glu Gln 260 265 270

Leu Glu Gly Lys Leu His Thr Tyr Ser Leu Phe Gly Leu Pro Arg Leu 275 280 285

Pro Arg Gly Leu Arg Phe Asp His Asp Ser Trp Glu Glu Glu Tyr Asp 290 295 300

Glu Asp Glu Asp Glu Asp Asn Ala Cys Leu Arg Leu Glu Asp Ser Trp 305 310 315 320

Arg Glu Leu lle Asp Gly His Glu Lys Leu Thr Arg Arg Gln Cys His 325 330 335

Gln Gln Glu Ala Val Trp Glu Leu Leu His Thr Glu Ala Ser Tyr lle 340 345 350

Arg Lys Leu Arg Val IIe IIe Asn Leu Phe Leu Cys Cys Leu Leu Asn 355 360 365

Leu Gln Glu Ser Gly Leu Leu Cys Glu Val Glu Ala Glu Arg Leu Phe 370 375 380

Ser Asn Ile Pro Glu Ile Ala Gln Leu His Arg Arg Leu Trp Ala Ser 385 390 395 400

Val Met Ala Pro Val Leu Glu Lys Ala Arg Arg Thr Arg Ala Leu Leu 405 410 415

Gln Pro Gly Asp Phe Leu Lys Gly Phe Lys Met Phe Gly Ser Leu Phe 420 425 430

Lys Pro Tyr lle Arg Tyr Cys Met Glu Glu Glu Gly Cys Met Glu Tyr 435 440 445

Met Arg Gly Leu Leu Arg Asp Asp Asp Leu Phe Arg Ala Tyr Ile Thr 455 Trp Ala Glu Lys His Pro Gln Cys Gln Arg Leu Lys Leu Ser Asp Met Leu Ala Lys Pro His Gln Arg Leu Thr Lys Tyr Pro Leu Leu Leu Lys 490 Ser Val Leu Arg Lys Thr Glu Glu Pro Arg Ala Lys Glu Ala Val Val Ala Met lle Gly Ser Val Glu Arg Phe lle His His Val Asn Ala Cys Met Arg Gin Arg Gin Giu Arg Gin Arg Leu Ala Ala Val Val Ser Arg lle Asp Ala Tyr Glu Val Val Glu Ser Ser Ser Asp Glu Val Asp Lys 555 Leu Leu Lys Glu Phe Leu His Leu Asp Leu Thr Ala Pro Ile Pro Gly Ala Ser Pro Glu Glu Thr Arg Gln Leu Leu Glu Gly Ser Leu Arg 585 Met Lys Glu Gly Lys Asp Ser Lys Met Asp Val Tyr Cys Phe Leu Phe Thr Asp Leu Leu Val Thr Lys Ala Val Lys Lys Ala Glu Arg Thr 615 Arg Val IIe Arg Pro Pro Leu Leu Val Asp Lys IIe Val Cys Arg Glu Leu Arg Asp Pro Gly Ser Phe Leu Leu lle Tyr Leu Asn Glu Phe His Ser Ala Val Gly Ala Tyr Thr Phe Gln Ala Ser Gly Gln Ala Leu Cys 660 665 Arg Gly Trp Val Asp Thr lle Tyr Asn Ala Gln Asn Gln Leu Gln Gln 680 685 Leu Arg Ala Gln Glu Pro Pro Gly Ser Gln Gln Pro Leu Gln Ser Leu 695 700 Glu Glu Glu Glu Asp Glu Gln Glu Glu Glu Glu Glu Glu Glu Glu Glu Glu Glu Gly Glu Asp Ser Gly Thr Ser Ala Ala Ser Ser Pro Thr lle Met Arg Lys Ser Ser Gly Ser Pro Asp Ser Gln His Cys Ala Ser 740

🖟 Leu Ala Met Val Val Val Glu 🖟 Asp Gly Ser Thr Gl 760 Thr Leu Ser Ser Pro Glu Phe Asp Ser Gly Pro Phe Ser Ser Gln Ser Asp Glu Thr Ser Leu Ser Thr Thr Ala Ser Ser Ala Thr Pro Thr Ser 800 795 Glu Leu Leu Pro Leu Gly Pro Val Asp Gly Arg Ser Cys Ser Met Asp Ser Ala Tyr Gly Thr Leu Ser Pro Thr Ser Leu Gln Asp Phe Val Ala 825 Pro Gly Pro Met Ala Glu Leu Val Pro Arg Ala Pro Glu Ser Pro Arg 845 835 Val Pro Ser Pro Pro Pro Ser Pro Arg Leu Arg Arg Thr Pro Val 855 Gln Leu Leu Ser Cys Pro Pro His Leu Leu Lys Ser Lys Ser Glu Ala Ser Leu Leu Gln Leu Leu Ala Gly Ala Gly Thr His Gly Thr Pro Ser 885 Ala Pro Ser Arg Ser Leu Ser Glu Leu Cys Leu Ala Val Pro Ala Pro 905 Gly lie Arg Thr Gln Gly Ser Pro Gln Glu Ala Gly Pro Ser Trp Asp 920 Cys Arg Gly Ala Pro Ser Pro Gly Ser Gly Pro Gly Leu Val Gly Cys 935 Leu Ala Gly Glu Pro Ala Gly Ser His Arg Lys Arg Cys Gly Asp Leu Pro Ser Gly Ala Ser Pro Arg Val Gln Pro Glu Pro Pro Pro Gly Val 975 965 Ser Ala Gln His Arg Lys Leu Thr Leu Ala Gln Leu Tyr Arg lle Arg 980 985 Thr Thr Leu Leu Leu Asn Ser Thr Leu Thr Ala Ser Glu Val

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<213> Homo sapiens

<220>

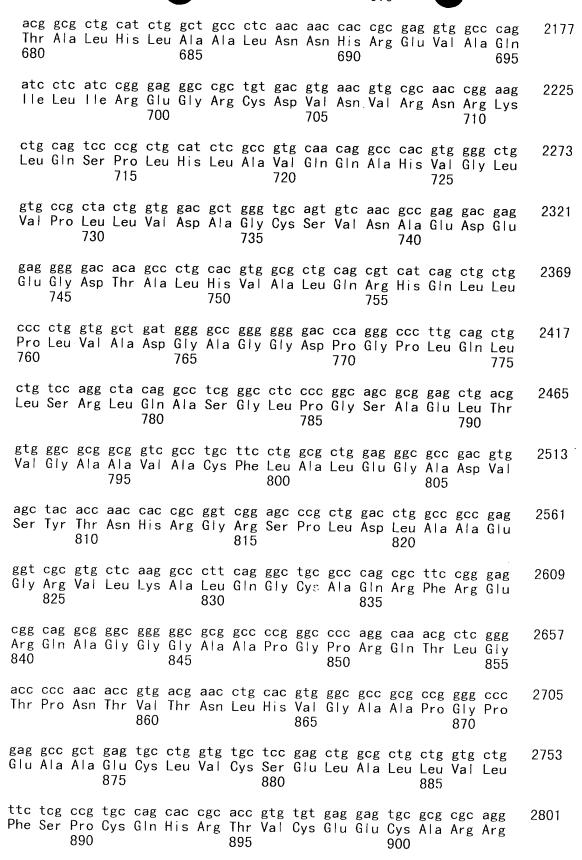
<221> CDS

<222> (93).. (3089)

| <400> 159   |                                   |                                   |                                 |                               |                       |  |  |  |  |  |  |  |
|---|-----------------------------------|-----------------------------------|---------------------------------|-------------------------------|-----------------------|--|--|--|--|--|--|--|
| agtgcccggt ggcccaggag ggcctgggag cccgaagccg tccccgagtc gctcctaggt 6 |                                   |                                   |                                 |                               |                       |  |  |  |  |  |  |  |
| cactggcgcg atgc   | gggccg tcctct                     |                                   | ggt tgg aa<br>Gly Trp Ly        |                               |                       |  |  |  |  |  |  |  |
| gct aga ggc cag<br>Ala Arg Gly Gln<br>10                            | tcc caa agt<br>Ser Gln Ser        | ctc cag gca<br>Leu Gln Ala<br>15  | Ser Gly Le                      | g cag ccc<br>u Gln Pro<br>O   | agg 161<br>Arg        |  |  |  |  |  |  |  |
| agc ctc aag gcg<br>Ser Leu Lys Ala<br>25                            | gcc cgg cgg<br>Ala Arg Arg<br>30  | gcg act gga<br>Ala Thr Gly        | cgg ccg ga<br>Arg Pro As<br>35  | c agg tcc<br>p Arg Ser        | cga 209<br>Arg        |  |  |  |  |  |  |  |
| gca gcc ccg ccc<br>Ala Ala Pro Pro<br>40                            | aac atg gac<br>Asn Met Asp<br>45  | cca gac ccc<br>Pro Asp Pro        | cag gcg gg<br>Gln Ala Gl<br>50  | c gtg cag<br>y Val Gln        | gtg 257<br>Val<br>55  |  |  |  |  |  |  |  |
| ggc atg cgg gtg<br>Gly Met Arg Val                                  | gtg cgc ggc<br>Val Arg Gly<br>60  | gtg gac tgg<br>Val Asp Trp<br>65  | Lys Trp Gl                      | c cag cag<br>y Gln Gln<br>70  | gac 305<br>Asp        |  |  |  |  |  |  |  |
| ggc ggc gag ggc<br>Gly Gly Glu Gly<br>75                            | ggc gtg ggc<br>Gly Val Gly        | acg gtg gtg<br>Thr Val Val<br>80  | gag ctt gg<br>Glu Leu Gl        | c cgc cac<br>y Arg His<br>85  | ggc 353<br>Gly        |  |  |  |  |  |  |  |
| agc ccc tcg aca<br>Ser Pro Ser Thr<br>90                            | ccc gac cgc<br>Pro Asp Arg        | aca gtg gtc<br>Thr Val Val<br>95  | gtg cag tg<br>Val Gln Tr<br>10  | p Asp Gln                     | ggc 401<br>Gly        |  |  |  |  |  |  |  |
| acg cgc acc aac<br>Thr Arg Thr Asn<br>105                           | tac cgc gcc<br>Tyr Arg Ala<br>110 | ggc tac cag<br>Gly Tyr Gln        | ggc gcg ca<br>Gly Ala Hi<br>115 | c gac ctg<br>s Asp Leu        | ctg 449<br>Leu        |  |  |  |  |  |  |  |
| ctg tac gac aac<br>Leu Tyr Asp Asn<br>120                           | gcc cag atc<br>Ala Gln lle<br>125 | ggc gtc cgg<br>Gly Val Arg        | cac ccc aa<br>His Pro As<br>130 | c atc atc<br>n lle lle        | tgt 497<br>Cys<br>135 |  |  |  |  |  |  |  |
| gac tgc tgc aag<br>Asp Cys Cys Lys                                  | aag cac ggg<br>Lys His Gly<br>140 | ctg cgg ggg<br>Leu Arg Gly<br>145 | Met Arg Tr                      | g aag tgc<br>p Lys Cys<br>150 | cgt 545<br>Arg        |  |  |  |  |  |  |  |
| gtg tgc ctg gac<br>Va  Cys Leu Asp<br>155                           | tac gac ctc<br>Tyr Asp Leu        | tgc acg cag<br>Cys Thr Gln<br>160 | tgc tac at<br>Cys Tyr Me        | g cac aac<br>t His Asn<br>165 | aag 593<br>Lys        |  |  |  |  |  |  |  |
| cat gag ctc gcc<br>His Glu Leu Ala<br>170                           | cac gcc ttc<br>His Ala Phe        | gac cgc tac<br>Asp Arg Tyr<br>175 | gag acc gc<br>Glu Thr Al<br>18  | a His Ser                     | cgc 641<br>Arg        |  |  |  |  |  |  |  |
| cct gtc aca ctg<br>Pro Val Thr Leu<br>185                           |                                   |                                   |                                 |                               |                       |  |  |  |  |  |  |  |
| ggc atc ttc cag<br>Gly lle Phe Gln                                  | gga gcg aag<br>Gly Ala Lys        | gtg gtg cga<br>Val Val Arg        | ggc ccc tt<br>Gly Pro Ph        | c tgg gag<br>e Trp Glu        | tgg 737<br>Trp        |  |  |  |  |  |  |  |

| ggc<br>Gly        | tca<br>Ser        | cag<br>Gln          | gat<br>Asp        | gga<br>Gly<br>220 | ggg<br>Gly        | gaa<br>Glu          | ggg<br>Gly        | aaa<br>Lys        | ccg<br>Pro<br>225 | ggc<br>Gly        | cgt<br>Arg          | gtg<br><b>Va</b> l | gtg<br>Val        | gac<br>Asp<br>230 | atc<br>lle        | 785  |
|-------------------|-------------------|---------------------|-------------------|-------------------|-------------------|---------------------|-------------------|-------------------|-------------------|-------------------|---------------------|--------------------|-------------------|-------------------|-------------------|------|
| cgt<br>Arg        | ggc<br>Gly        | tgg<br>Trp          | gat<br>Asp<br>235 | gtg<br>Val        | gag<br>Glu        | aca<br>Thr          | ggc<br>Gly        | cgg<br>Arg<br>240 | agt<br>Ser        | gtg<br>Val        | gcc<br>Ala          | agc<br>Ser         | gtg<br>Val<br>245 | acg<br>Thr        | tgg<br>Trp        | 833  |
| gct<br>Ala        | gat<br>Asp        | ggt<br>Gly<br>250   | acc<br>Thr        | acc<br>Thr        | aat<br>Asn        | gtg<br>Val          | tac<br>Tyr<br>255 | cgt<br>Arg        | gtg<br>Val        | ggc<br>Gly        | cac<br>His          | aag<br>Lys<br>260  | ggc<br>Gly        | aag<br>Lys        | gtg<br>Val        | 881  |
| gac<br>Asp        | ctc<br>Leu<br>265 | aag<br>Lys          | tgt<br>Cys        | gtg<br>Val        | ggc<br>Gly        | gag<br>Glu<br>270   | gca<br>Ala        | gcg<br>Ala        | ggc<br>Gly        | ggc<br>Gly        | ttc<br>Phe<br>275   | tac<br>Tyr         | tac<br>Tyr        | aag<br>Lys        | gac<br>Asp        | 929  |
| cac<br>His<br>280 | ctc<br>Leu        | cca<br>Pro          | agg<br>Arg        | ctc<br>Leu        | ggc<br>Gly<br>285 | aag<br>Lys          | ccg<br>Pro        | gcg<br>Ala        | gag<br>Glu        | ctg<br>Leu<br>290 | cag<br>G n          | cgc<br>Arg         | agg<br>Arg        | gtg<br>Val        | agt<br>Ser<br>295 | 977  |
| gct<br>Ala        | gac<br>Asp        | agc<br>Ser          | cag<br>Gln        | ccc<br>Pro<br>300 | ttc<br>Phe        | cag<br>Gln          | cac<br>His        | ggg<br>Gly        | gac<br>Asp<br>305 | aag<br>Lys        | gtc<br>Val          | aag<br>Lys         | tgt<br>Cys        | ctg<br>Leu<br>310 | ctg<br>Leu        | 1025 |
| gac<br>Asp        | act<br>Thr        | gat<br>Asp          | gtc<br>Val<br>315 | ctg<br>Leu        | cgg<br>Arg        | gag<br>Glu          | atg<br>Met        | cag<br>Gln<br>320 | gaa<br>Glu        | ggc<br>Gly        | cac<br>His          | ggc<br>Gly         | ggc<br>Gly<br>325 | tgg<br>Trp        | aac<br>Asn        | 1073 |
| ccc<br>Pro        | agg<br>Arg        | atg<br>Met<br>330   | gcg<br>Ala        | gag<br>Glu        | ttt<br>Phe        | atc<br>He           | gga<br>Gly<br>335 | cag<br>Gln        | acg<br>Thr        | ggc<br>Gly        | acc<br>Thr          | gtg<br>Val<br>340  | cat<br>His        | cgt<br>Arg        | atc<br>lle        | 1121 |
| acg<br>Thr        | gac<br>Asp<br>345 | Arg                 | ggg<br>Gly        | gac<br>Asp        | gtg<br>Val        | cgc<br>Arg<br>350   | Val               | cag<br>Gln        | ttc<br>Phe        | aac<br>Asn        | cac<br>His<br>355   | gag<br>Glu         | acg<br>Thr        | cgc<br>Arg        | tgg<br>Trp        | 1169 |
| acc<br>Thr<br>360 | Phe               | cac<br>His          | ccc<br>Pro        | ggg<br>Gly        | gcg<br>Ala<br>365 | Leu                 | acc<br>Thr        | Lys               | His               | His               | Ser                 | ttc<br>Phe         | irp               | val               | GIY               | 1217 |
| gac<br>Asp        | gtg<br>Val        | gtc<br>Val          | cgg<br>Arg        | gto<br>Val<br>380 | He                | ggc                 | gac<br>Asp        | ctt<br>Leu        | gac<br>Asp<br>385 | Inr               | gtg<br>Val          | aag<br>Lys         | cgg<br>Arg        | ctg<br>Leu<br>390 | cag<br>Gln        | 1265 |
| gct<br>Ala        | ggg<br>Gly        | cat<br>His          | ggc<br>Gly<br>395 | / Glu             | g tgg<br>i Trp    | ; acg<br>Thr        | gac<br>Asp        | gac<br>Asp<br>400 | Met               | gcc               | cct<br>Pro          | gcc<br>Ala         | ctg<br>Leu<br>405 | l GIY             | cgc<br>Arg        | 1313 |
| gto<br>Val        | ggg<br>Gly        | g aag<br>Lys<br>410 | : Val             | g gtg<br>Val      | g aaa<br>Lys      | gtg<br>Val          | ttt<br>Phe<br>415 | e Gly             | a gad<br>⁄ Asp    | ggg<br>Gly        | g aac<br>/ Asr      | ctg<br>Leu<br>420  | ı Arg             | gta<br>g Val      | gca<br>Ala        | 1361 |
| gto<br>Val        | gct<br>Ala<br>425 | a Gly               | cag<br>Glr        | g ogg<br>n Arg    | g tgg<br>g Trp    | g acc<br>Thr<br>430 | Phe               | ago<br>e Sei      | c ccc<br>Pro      | tco<br>Sei        | tgo<br>r Cys<br>435 | s Lei              | g gtg<br>i Val    | g gco<br>  Ala    | tac<br>Tyr        | 1409 |

|        |                   |                   |                   |                   | 4                 |                   |                   |                   |                   |                   |                   |                   |                   |                   | <b>\</b>          |                   |      |
|--------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| Α      | gg<br>rg<br>40    | ccc<br>Pro        | gag<br>Glu        | gag<br>Glu        | gat<br>Asp        | scc<br>Ala<br>445 | aac<br>Asn        | ctg<br>Leu        | gac<br>Asp        | gtg<br>Val        | gcc<br>Ala<br>450 | gag<br>Glu        | cgc<br>Arg        | g<br>Ala          | cgg<br>Arg        | gag<br>Glu<br>455 | 1457 |
| A      | ac<br>sn          | aaa<br>Lys        | agc<br>Ser        | tca<br>Ser        | ctg<br>Leu<br>460 | agc<br>Ser        | gtg<br>Val        | gcc<br>Ala        | ctg<br>Leu        | gac<br>Asp<br>465 | aag<br>Lys        | ctt<br>Leu        | cgg<br>Arg        | gcc<br>Ala        | cag<br>Gln<br>470 | aag<br>Lys        | 1505 |
| S      | gt                | gac<br>Asp        | cca<br>Pro        | gag<br>Glu<br>475 | cac<br>His        | ccg<br>Pro        | gga<br>Gly        | agg<br>Arg        | ctg<br>Leu<br>480 | gtg<br>Val        | gtg<br>Val        | gag<br>Glu        | gtg<br>Val        | gcg<br>Ala<br>485 | ctg<br>Leu        | ggt<br>Gly        | 1553 |
| A      | ac<br>sn          | gca<br>Ala        | gcc<br>Ala<br>490 | cgg<br>Arg        | gct<br>Ala        | ctg<br>Leu        | gac<br>Asp        | ctg<br>Leu<br>495 | ctg<br>Leu        | cgg<br>Arg        | agg<br>Arg        | cgc<br>Arg        | cca<br>Pro<br>500 | gag<br>Glu        | caa<br>Gln        | gtg<br>Val        | 1601 |
| g<br>A | gac<br>Nsp        | acc<br>Thr<br>505 | aag<br>Lys        | aac<br>Asn        | caa<br>Gln        | ggc<br>Gly        | agg<br>Arg<br>510 | acc<br>Thr        | gct<br>Ala        | ctg<br>Leu        | caa<br>Gln        | gtg<br>Val<br>515 | gct<br>Ala        | gcc<br>Ala        | tac<br>Tyr        | ctg<br>Leu        | 1649 |
| (      | ggc<br>Hy<br>520  | cag<br>Gln        | gtg<br>Val        | gag<br>Glu        | ttg<br>Leu        | ata<br>Ile<br>525 | cgg<br>Arg        | ctg<br>Leu        | ctg<br>Leu        | cta<br>Leu        | caa<br>Gln<br>530 | gcc<br>Ala        | agg<br>Arg        | gcg<br>Ala        | ggc<br>Gly        | gtg<br>Val<br>535 | 1697 |
| Ę      | gac<br>\sp        | ctg<br>Leu        | ccg<br>Pro        | gac<br>Asp        | gac<br>Asp<br>540 | gag<br>Glu        | ggc<br>Gly        | aac<br>Asn        | acg<br>Thr        | gca<br>Ala<br>545 | ctg<br>Leu        | cac<br>His        | tac<br>Tyr        | gcg<br>Ala        | gcc<br>Ala<br>550 | ctg<br>Leu        | 1745 |
| (      | ggg<br>Gly        | aac<br>Asn        | cag<br>Gln        | ccc<br>Pro<br>555 | gag<br>Glu        | gcc<br>Ala        | acc<br>Thr        | agg<br>Arg        | gtg<br>Val<br>560 | ctc<br>Leu        | ctg<br>Leu        | agt<br>Ser        | gct<br>Ala        | ggg<br>Gly<br>565 | tgc<br>Cys        | cgg<br>Arg        | 1793 |
| į      | gcg<br>Na         | gac<br>Asp        | gcc<br>Ala<br>570 | atc<br>Ile        | aac<br>Asn        | agc<br>Ser        | acc<br>Thr        | cag<br>Gln<br>575 | agc<br>Ser        | aca<br>Thr        | gca<br>Ala        | ctg<br>Leu        | cac<br>His<br>580 | gtg<br>Val        | gcc<br>Ala        | gtg<br>Val        | 1841 |
| (      | cag<br>G n        | agg<br>Arg<br>585 | ggc<br>Gly        | ttc<br>Phe        | ctg<br>Leu        | gag<br>Glu        | gtg<br>Val<br>590 | gtg<br>Val        | cgg<br>Arg        | gcc<br>Ala        | ctg<br>Leu        | tgt<br>Cys<br>595 | gag<br>Glu        | cgc<br>Arg        | ggc<br>Gly        | tgt<br>Cys        | 1889 |
| 1      | gac<br>Asp<br>300 | gtc<br>Val        | aac<br>Asn        | ctg<br>Leu        | ccc<br>Pro        | gac<br>Asp<br>605 | gcc<br>Ala        | cac<br>His        | tcg<br>Ser        | gac<br>Asp        | acg<br>Thr<br>610 | ccc<br>Pro        | ctg<br>Leu        | cac<br>His        | tcc<br>Ser        | gcc<br>Ala<br>615 | 1937 |
| ;      | atc<br>Ile        | tcg<br>Ser        | gcg<br>Ala        | ggc<br>Gly        | act<br>Thr<br>620 | gga<br>Gly        | gcc<br>Ala        | agc<br>Ser        | ggc<br>Gly        | att<br>lle<br>625 | Val               | gag<br>Glu        | gtc<br>Val        | ctc<br>Leu        | acg<br>Thr<br>630 | Glu               | 1985 |
| 1      | gtg<br>Val        | cca<br>Pro        | aac<br>Asn        | atc<br>Ile<br>635 | Asp               | gtt<br>Val        | acc<br>Thr        | gcc<br>Ala        | acc<br>Thr<br>640 | Asn               | agc<br>Ser        | cag<br>Gln        | ggt<br>Gly        | ttc<br>Phe<br>645 | acc<br>Thr        | ctg<br>Leu        | 2033 |
|        | ctg<br>Leu        | cac<br>His        | cat<br>His<br>650 | Ala               | tcc<br>Ser        | ctc<br>Leu        | aag<br>Lys        | ggt<br>Gly<br>655 | His               | gcg<br>Ala        | cta<br>Leu        | gct<br>Ala        | gtg<br>Val<br>660 | Arg               | aag<br>Lys        | att               | 2081 |
|        | ctg<br>Leu        | gct<br>Ala        | cgg<br>Arg        | gcg<br>Ala        | cgg<br>Arg        | cag<br>G n        | ctg<br>Leu        | gtg<br>Val        | gac<br>Asp        | gcc<br>Ala        | aag<br>Lys        | aag<br>Lys        | gag<br>Glu        | gac<br>Asp        | ggc<br>Gly        | ttc<br>Phe        | 2129 |



| Met  | aag<br>Lys<br>905                                 | aag<br>Lys                                       | tgc<br>Cys                     | ate   | g<br>Arg                       | tgc<br>Cys<br>910              | Gln                            | gtg<br>Val                     | gto<br>Val                     | gtc<br>Val                            | agc<br>Ser<br>915                     | Lys                                   | Lys                            | ctg<br>Leu                                  | g cgc<br>i Arg     | 2849 |
|--|---|--|--------------------------------|---|--------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|--------------------------------|---|--------------------|------|
| cca<br>Pro<br>920                                | gac<br>Asp  | ggc<br>Gly                                       | tct<br>Ser                     | gag<br>Glu                                  | gtg<br>Val<br>925              | Ala                            | agc<br>Ser                     | gcc<br>Ala                     | gcc<br>Ala                     | Pro<br>930                            | Ala                                   | ccc<br>Pro                            | ggo                            | ccg<br>Pro                                  | ccg<br>Pro<br>935  | 2897 |
|  |   |  |                                |   |                                |                                |                                |                                |                                | Tyr                                   |                                       |                                       |                                |   | gaa<br>Glu         | 2945 |
| cgc<br>Arg                                       | atc<br>Ile  | acc<br>Thr                                       | tgc<br>Cys<br>955              | ccc<br>Pro                                  | atc<br>Ile                     | tgc<br>Cys                     | atc<br>He                      | gac<br>Asp<br>960              | agg<br>Arg                     | cac<br>His                            | atc<br>lle                            | cgc<br>Arg                            | ctc<br>Leu<br>965              | Val   | ttc<br>Phe         | 2993 |
| cag<br>Gln                                       | tgc<br>Cys  | ggc<br>Gly<br>970                                | cac<br>His                     | ggc<br>Gly                                  | gca<br>Ala                     | tgc<br>Cys                     | gcc<br>Ala<br>975              | ccc<br>Pro                     | tgc<br>Cys                     | ggc<br>Gly                            | tcc<br>Ser                            | gcg<br>Ala<br>980                     | ctc<br>Leu                     | agc<br>Ser                                  | gcc<br>Ala         | 3041 |
| tgc<br>Cys                                       | ccc<br>Pro<br>985                                 | atc<br>Ile                                       | tgc<br>Cys                     | cgc<br>Arg                                  | cag<br>G n                     | ccc<br>Pro<br>990              | atc<br>Ile                     | cgc<br>Arg                     | gac<br>Asp                     | cgc<br>Arg                            | atc<br>lle<br>995                     | cag<br>G n                            | atc<br>  e                     | ttc<br>Phe                                  | gtg<br>Val         | 3089 |
| tgag   | gccgc   | gc c   | gtcc                           | gcce  | gc gc                          | ccga                           | agctg                          | g cct                          | tcg                            | cgtg                                  | ccc                                   | ccgc                                  | cct                            | gtgt  | tttata             | 3149 |
| aaaa   | igaaa   | ıga t  | toto                           | ggat  | <u>-</u>                       |                                |                                |                                |                                |                                       |                                       |                                       |                                |   |                    | 3168 |
|  |   |  |                                |   |                                |                                |                                |                                |                                |                                       |                                       |                                       |                                |   |                    |      |
| <211<br><212                                     | )> 16<br>> 99<br>!> PR<br>!> Ho                   | 9<br>T   | apie                           | ns  |                                |                                |                                |                                |                                |                                       |                                       |                                       |                                |   |                    |      |
| <211<br><212<br><213<br><400                     | > 99<br>!> PR                                     | 9<br>T<br>mo s                                   |                                |   | Ser                            | Glu                            | Ala                            | Arg                            | G y<br>10                      | Gln                                   | Ser                                   | Gln                                   | Ser                            | Leu<br>15                                   | Gln                |      |
| <211<br><212<br><213<br><400<br>Met<br>1         | > 99<br>> PR<br>> Ho<br>> 16                      | 9<br>T<br>mo s<br>O<br>Trp                       | Lys                            | Pro<br>5                                    |                                |                                |                                |                                | 10                             |                                       |                                       |                                       |                                | 15  |                    |      |
| <211<br><212<br><213<br><400<br>Met<br>1         | > 99<br>> PR<br>> Ho<br>> 16<br>Gly<br>Ser        | 9<br>T<br>mo s<br>O<br>Trp                       | Lys<br>Leu<br>20               | Pro<br>5<br>Gln                             | Pro                            | Arg                            | Ser                            | Leu<br>25                      | 10<br>Lys                      | Ala                                   | Ala                                   | Arg                                   | Arg<br>30                      | 15<br>Ala                                   | Thr                |      |
| <211<br><212<br><213<br><400<br>Met<br>1         | > 99<br>> PR<br>> Ho<br>> 16<br>Gly<br>Ser        | g<br>T<br>mo s<br>O<br>Trp<br>Gly<br>Pro         | Lys<br>Leu<br>20<br>Asp        | Pro<br>5<br>Gln<br>Arg                      | Pro<br>Ser                     | Arg<br>Arg                     | Ser<br>Ala<br>40               | Leu<br>25<br>Ala               | 10<br>Lys<br>Pro               | Ala<br>Pro                            | Ala<br>Asn                            | Arg<br>Met<br>45                      | Arg<br>30<br>Asp               | 15<br>Ala<br>Pro                            | Thr<br>Asp         |      |
| <211<br><212<br><213<br><400<br>Met<br>1<br>Ala  | > 99<br>> PR<br>> Ho<br>> 16<br>Gly<br>Ser<br>Arg | 9<br>Tomo s<br>O<br>Trp<br>Gly<br>Pro 2<br>35    | Lys<br>Leu<br>20<br>Asp        | Pro<br>5<br>Gln<br>Arg<br>Val               | Pro<br>Ser<br>Gln              | Arg<br>Arg<br>Val<br>55        | Ser<br>Ala<br>40<br>Gly        | Leu<br>25<br>Ala<br>Met        | 10<br>Lys<br>Pro<br>Arg        | Ala<br>Pro<br>Val                     | Ala<br>Asn<br>Val<br>60               | Arg<br>Met<br>45<br>Arg               | Arg<br>30<br>Asp<br>Gly        | 15<br>Ala<br>Pro<br>Val                     | Thr<br>Asp<br>Asp  |      |
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| <211 <212 <213 <400 Met     1 Ala Gly Pro Trp 65 | > 99 > PR > Ho > 16 Gly Ser Arg 50 Lys            | 9 Trp Gly Pro 35 Ala (                           | Lys<br>Leu<br>20<br>Asp<br>Gly | Pro<br>5<br>Gln<br>Arg<br>Val<br>Gln<br>Arg | Pro<br>Ser<br>Gln<br>Gln<br>70 | Arg<br>Arg<br>Val<br>55<br>Asp | Ser<br>Ala<br>40<br>Gly<br>Gly | Leu<br>25<br>Ala<br>Met<br>Gly | Lys Pro Arg Glu Ser 90         | Ala<br>Pro<br>Val<br>Gly<br>75<br>Thr | Ala<br>Asn<br>Val<br>60<br>Gly<br>Pro | Arg<br>Met<br>45<br>Arg<br>Val<br>Asp | Arg<br>30<br>Asp<br>Gly<br>Gly | 15<br>Ala<br>Pro<br>Val<br>Thr<br>Thr<br>95 | Thr Asp Asp Val 80 |      |

| Ar           | g His<br>130 | s Pr<br>O  | o As         | n H          | e Tle        | Cys<br>135 | s Ası      | o Cy:       | s Cy:        | s Lys        | 140         | His        | s GT       | Lei          | u Arg        |
|--------------|--------------|------------|--------------|--------------|--------------|------------|------------|-------------|--------------|--------------|-------------|------------|------------|--------------|--------------|
| G I y<br>145 | y Met        | t Ar       | g Tr         | p Ly:        | s Cys<br>150 | Arg        | g Va       | Cy:         | s Lei        | u Asp<br>155 |             | Asp        | Lei        | ı Cys        | s Thr<br>160 |
| Glr          | n Cys        | з Ту       | r Me         | t His<br>165 | s Asn        | Lys        | : His      | s Glu       | ب Leu<br>170 |              | a His       | Ala        | a Phe      | e Asp<br>175 | o Arg        |
| Tyr          | Glu          | ı Th       | r Ala<br>180 | a His<br>O   | s Ser        | Arg        | Pro        | Va l<br>185 | l Thr        | Lei          | l Ser       | Pro        | Arg<br>190 |              | n Gly        |
| Leu          | ı Pro        | 19         | g 11e<br>5   | e Pro        | ) Leu        | Arg        | Gly<br>200 | /   e       | e Phe        | e Gin        | Gly         | Ala<br>205 |            | Val          | Val          |
| Arg          | Gly<br>210   | / Pro      | ) Phe        | e Trp        | Glu          | Trp<br>215 | Gly        | ' Ser       | Glr          | n Asp        | Gly<br>220  | Gly        | Glu        | ı Gly        | / Lys        |
| Pro<br>225   | Gly          | ⁄ Arg      | g Val        | Val          | Asp<br>230   | lle        | Arg        | Gly         | Trp          | Asp<br>235   | Val         | Glu        | Thr        | Gly          | Arg<br>240   |
| Ser          | Val          | Ala        | a Ser        | Val<br>245   |              | Trp        | Ala        | Asp         | G y<br>250   |              | Thr         | Asn        | Val        | Tyr<br>255   | Arg          |
| Val          | Gly          | His        | 260          | Gly          | Lys          | Val        | Asp        | Leu<br>265  |              | Cys          | Val         | Gly        | Glu<br>270 |              | Ala          |
| Gly          | Gly          | Phe<br>275 | Tyr          | Tyr          | Lys          | Asp        | His<br>280 | Leu         | Pro          | Arg          | Leu         | Gly<br>285 | Lys        | Pro          | Ala          |
| Glu          | Leu<br>290   | Gln        | Arg          | Arg          | Val          | Ser<br>295 | Ala        | Asp         | Ser          | Gln          | Pro<br>300  | Phe        | Gln        | His          | Gly          |
| Asp<br>305   | Lys          | Val        | Lys          | Cys          | Leu<br>310   | Leu        | Asp        | Thr         | Asp          | Val<br>315   | Leu         | Arg        | Glu        | Met          | Gin<br>320   |
| Glu          | Gly          | His        | Gly          | Gly<br>325   | Trp          | Asn        | Pro        | Arg         | Met<br>330   | Ala          | Glu         | Phe        | lle        | Gly<br>335   | Gln          |
| Thr          | Gly          | Thr        | Val<br>340   | His          | Arg          | lle        | Thr        | Asp<br>345  | Arg          | Gly          | Asp         | Val        | Arg<br>350 | Val          | Gln          |
| Phe          | Asn          | His<br>355 | Glu          | Thr          | Arg          | Trp        | Thr<br>360 | Phe         | His          | Pro          |             | Ala<br>365 | Leu        | Thr          | Lys          |
| His          | His<br>370   | Ser        | Phe          | Trp          | Val          | G∣y<br>375 | Asp        | Val         | Val          | Arg          | Va l<br>380 | He         | Gly        | Asp          | Leu          |
| Asp<br>385   | Thr          | Val        | Lys          | Arg          | Leu<br>390   | Gln        | Ala        | Gly         | His          | Gly<br>395   | Glu         | Trp        | Thr        | Asp          | Asp<br>400   |
| Met          | Ala          | Pro        | Ala          | Leu<br>405   | Gly          | Arg        | Val        | Gly         | Lys<br>410   | Val          | Val         | Lys        | Val        | Phe<br>415   | Gly          |
| Asp          | Gly          | Asn        | Leu<br>420   | Arg          | Val          | Ala        | Val        | Ala<br>425  | Gly          | Gln          | Arg         |            | Thr<br>430 | Phe          | Ser          |

Pro Ser Cys Leu Valeria Tyr Arg Pro Glu Glu Asp Ala Leu Asp 435

Val Ala Glu Arg Ala Arg Glu Asn Lys Ser Ser Leu Ser Val Ala Leu 450 455 460

Asp Lys Leu Arg Ala Gln Lys Ser Asp Pro Glu His Pro Gly Arg Leu 465 470 475 480

Val Val Glu Val Ala Leu Gly Asn Ala Ala Arg Ala Leu Asp Leu Leu 485 490 495

Arg Arg Arg Pro Glu Gln Val Asp Thr Lys Asn Gln Gly Arg Thr Ala 500 505 510

Leu Gln Val Ala Ala Tyr Leu Gly Gln Val Glu Leu Ile Arg Leu Leu 515 520 525

Leu Gln Ala Arg Ala Gly Val Asp Leu Pro Asp Asp Glu Gly Asn Thr 530 540

Ala Leu His Tyr Ala Ala Leu Gly Asn Gln Pro Glu Ala Thr Arg Val 545 550 555 560

Leu Leu Ser Ala Gly Cys Arg Ala Asp Ala Ile Asn Ser Thr Gln Ser 565 570 575

Thr Ala Leu His Val Ala Val Gln Arg Gly Phe Leu Glu Val Val Arg 580 585 590

Ala Leu Cys Glu Arg Gly Cys Asp Val Asn Leu Pro Asp Ala His Ser 595 600 605

Asp Thr Pro Leu His Ser Ala IIe Ser Ala Gly Thr Gly Ala Ser Gly 610 620

lle Val Glu Val Leu Thr Glu Val Pro Asn lle Asp Val Thr Ala Thr 625 630 635 640

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Ala Leu Ala Val Arg Lys Ile Leu Ala Arg Ala Arg Gln Leu Val Asp 660 665 670

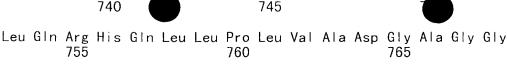
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Val Asn Val Arg Asn Arg Lys Leu Gln Ser Pro Leu His Leu Ala Val 705 710 715 720

Gln Gln Ala His Val Gly Leu Val Pro Leu Leu Val Asp Ala Gly Cys 725 730 735

Ser Val Asn Ala Glu Asp Glu Glu Gly Asp Thr Ala Leu His Val Ala



Asp Pro Gly Pro Leu Gln Leu Leu Ser Arg Leu Gln Ala Ser Gly Leu

Pro Gly Ser Ala Glu Leu Thr Val Gly Ala Ala Val Ala Cys Phe Leu 795

Ala Leu Glu Gly Ala Asp Val Ser Tyr Thr Asn His Arg Gly Arg Ser

Pro Leu Asp Leu Ala Ala Glu Gly Arg Val Leu Lys Ala Leu Gln Gly

Cys Ala Gin Arg Phe Arg Glu Arg Gln Ala Gly Gly Ala Ala Pro

Gly Pro Arg Gln Thr Leu Gly Thr Pro Asn Thr Val Thr Asn Leu His

Val Gly Ala Ala Pro Gly Pro Glu Ala Ala Glu Cys Leu Val Cys Ser

Glu Leu Ala Leu Leu Val Leu Phe Ser Pro Cys Gln His Arg Thr Val

Cys Glu Glu Cys Ala Arg Arg Met Lys Lys Cys Ile Arg Cys Gln Val 905

Val Val Ser Lys Lys Leu Arg Pro Asp Gly Ser Glu Val Ala Ser Ala

Ala Pro Ala Pro Gly Pro Pro Arg Gln Leu Val Glu Glu Leu Gln Ser

Arg Tyr Arg Gln Met Glu Glu Arg lle Thr Cys Pro lle Cys lle Asp 955

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| agtgcccggt | ggcccaggag | ggcctgggag | cccgaagccg | tccccgagtc gctcctaggt | 60  |
|------------|------------|------------|------------|-----------------------|-----|
| cactggcgcg | atgcgggccg | tcctctcggc | tg atg ggt | tgg aag ccc agc gag   | 113 |

| cactggcgcg atgc | gggccg tcctctcggc | t g | atg<br>Met | ggt<br>Gly | tgg<br>Trp | aag<br>Lvs | ccc<br>Pro | agc<br>Ser | gag<br>Glu | 113 |
|-----------------|-------------------|-----|------------|------------|------------|------------|------------|------------|------------|-----|
|                 |                   |     | 1          |            | •          | •          | 5          |            |            |     |

| gct aga ggc cag tcc | caa agt ctc cag | gca tca ggg ctg cag ccc ag | g 161 |
|---------------------|-----------------|----------------------------|-------|
| Ala Arg Gly Gln Ser | Gln Ser Leu Gln | Ala Ser Gly Leu Gln Pro Ar |       |
| 10                  | 15              | 20                         | 5     |

| agc ctc aag gcg g<br>Ser Leu Lys Ala A<br>25 | cc cgg cgg gcg<br>la Arg Arg Ala<br>30 | act gga cgg ccg gac agg t<br>Thr Gly Arg Pro Asp Arg S<br>35 | cc cga 209<br>er Arg |
|--|--|--|----------------------|
|--|--|--|----------------------|

| gca gcc ccg ccc aa | c atg gac cc  | gac ccc cag gcg ggc | gtg cag gtg 257 |
|--------------------|---------------|---------------------|-----------------|
| Ala Ala Pro Pro As | n Met Asp Pro | Asp Pro Gin Ala Gly | Val Gln Val     |
| 40                 | 45            | 50                  | 55              |

| ggc atg cgg gtg gtg cgc<br>Gly Met Arg Val Val Arg<br>60 | ggc gtg gac tgg aag tgg<br>Gly Val Asp Trp Lys Trp<br>65 | ggc cag cag gac 305<br>Gly Gln Gln Asp |
|--|--|--|
|--|--|--|

| ggc | ggc | gag | ggc | ggc | gtg | ggc | acg | gtg | gtg | gag | ctt | ggc | cgc | cac | ggc | 353 |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Gly | Gly | Glu | Gly | Gly | Val | Gly | Thr | Val | Val | Glu | Leu | Gly | Arg | His | Gly |     |
|     |     |     | 75  |     |     |     |     | 80  |     |     |     | •   | 85  |     | ,   |     |

| agc ccc tcg aca ccc | gac cgc aca gtg gtc | gtg cag tgg gac cag ggc | 401 |
|---------------------|---------------------|-------------------------|-----|
| Ser Pro Ser Thr Pro | Asp Arg Thr Val Val | Val Gln Trp Asp Gln Gly |     |
| 90                  | 95                  | 100                     |     |

| acg cgc acc aac<br>Thr Arg Thr Asr<br>105 | tac cgc gcc ggc<br>Tyr Arg Ala Gly<br>110 | ac cag ggc gcg ca<br>Tyr Gln Gly Ala Hi | c gac ctg ctg 449<br>s Asp Leu Leu |
|---|---|---|------------------------------------|
|---|---|---|------------------------------------|

| ctg<br>Leu<br>120 | tac<br>Tyr | gac<br>Asp | aac<br>Asn | gcc<br>Ala | cag<br>Gln<br>125 | atc<br>lle | ggc<br>Gly | gtc<br>Val | cgg<br>Arg | His | ccc<br>Pro | aac<br>Asn | atc<br>lle | atc<br>lle | tgt<br>Cys | 497 |
|-------------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|-----|------------|------------|------------|------------|------------|-----|
| 120               |            |            |            |            | 125               |            |            |            |            | 130 |            |            |            |            | 135        |     |

| gac tgc tgc aag<br>Asp Cys Cys Lys | aag cac<br>Lys His<br>140 | ggg ctg cgg<br>Gly Leu Arg | ggg atg cgc tg<br>Gly Met Arg Ti<br>145 | gg aag tgc cgt 54<br>rp Lys Cys Arg<br>150 |
|------------------------------------|---------------------------|----------------------------|---|--|
|------------------------------------|---------------------------|----------------------------|---|--|

| gtg tgc ctg gac tac<br>Val Cys Leu Asp Tyr | gac ctc tgc<br>Asp Leu Cys | Thr Gln Cys Tyr | atg cac aac aag<br>Met His Asn Lys | 593 |
|--|----------------------------|-----------------|------------------------------------|-----|
| 155  |                            | 160             | 165                                |     |

| cct gtc<br>Pro Val<br>185 | Ihr | ctg<br>Leu | agt<br>Ser | ccc<br>Pro | cgc<br>Arg<br>190 | cag<br>Gln | ggc<br>Gly | ctc<br>Leu | ccg<br>Pro | agg<br>Arg<br>195 | atc<br>lle | cca<br>Pro | cta<br>Leu | agg<br>Arg | 689 |
|---------------------------|-----|------------|------------|------------|-------------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|-----|
|---------------------------|-----|------------|------------|------------|-------------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|-----|

|                       |                            |                    |                            |                     |                   |                   |                   |                   |                     |                       | •                 |                       |                   | _                   |                       |      |
|-----------------------|----------------------------|--------------------|----------------------------|---------------------|-------------------|-------------------|-------------------|-------------------|---------------------|-----------------------|-------------------|-----------------------|-------------------|---------------------|-----------------------|------|
|                       | gc at<br>y II<br>)O        |                    |                            |                     |                   | a Lys             | g gtg<br>s Val    | g gtg<br>I Val    | g oga<br>I Arg      | a ggo<br>g Gly<br>210 | y Pr              | c tt<br>o Ph          | e T               | ga,                 | g tgg<br>u Trp<br>215 | 737  |
| gg<br>G l             | gc tc<br>y Se              | a ca<br>r Gl       | g ga<br>n As               | t gg<br>p Gl<br>22  | y Gly             | g gaa<br>/ Glu    | aggg<br>uGly      | g aaa<br>/ Lys    | e ccg<br>Pro<br>225 | Gly                   | c cg<br>y Ar      | t gt<br>g Va          | g gt<br>I Va      | g gad<br>Ası<br>230 | c atc<br>p lle<br>O   | 785  |
| cg<br>Ar              | t gg<br>g Gl               | c tg<br>y Tr       | g ga<br>p As<br>23         | p Va                | g gag<br>I Glu    | g aca<br>ı Thr    | aggo<br>Gly       | cgg<br>Arg<br>240 | g Ser               | gtg<br>Vai            | g gc              | c ago<br>a Sei        | c gt<br>Va<br>245 | Thi                 | g tgg<br>r Trp        | 833  |
| gc<br>Al              | t ga <sup>.</sup><br>a Ası | t gg<br>b G1<br>25 | y Th                       | c aco<br>r Thi      | c aat<br>r Asr    | gtg<br>Val        | tac<br>Tyr<br>255 | Arg               | gtg<br>Val          | g ggc<br>Gly          | cae<br>/ His      | c aag<br>s Lys<br>260 | s Gly             | c aag<br>/ Lys      | g gtg<br>s Val        | 881  |
| ga<br>As              | c cto<br>p Leo<br>265      | ı Ly:              | g tg <sup>.</sup><br>s Cy: | t gtg<br>s Val      | g ggc<br>  Gly    | gag<br>Glu<br>270 | Ala               | gcg<br>Ala        | ggc                 | ggc                   | tto<br>Phe<br>275 | e Tyr                 | tac<br>Tyr        | aag<br>Lys          | g gac<br>s Asp        | 929  |
| са<br>Ні<br>28        | s Lei                      | c cca<br>u Pro     | a agg<br>o Arg             | g cto<br>g Leu      | ggc<br>Gly<br>285 | Lys               | ccg<br>Pro        | gcg<br>Ala        | gag<br>Glu          | ctg<br>Leu<br>290     | Glr               | g cgc<br>n Arg        | agg<br>Arg        | g gtg<br>Val        | g agt<br>Ser<br>295   | 977  |
| gc<br>Al              | t gac<br>a Asp             | ago<br>Ser         | cag<br>Glr                 | g ccc<br>Pro<br>300 | Phe               | cag<br>Gln        | cac<br>His        | ggg<br>Gly        | gac<br>Asp<br>305   | aag<br>Lys            | gtc<br>Val        | aag<br>Lys            | tgt<br>Cys        | ctg<br>Leu<br>310   | ctg<br>Leu            | 1025 |
| ga<br>As <sub>l</sub> | c act<br>o Thr             | gat<br>Asp         | gto<br>Val                 | Leu                 | cgg<br>Arg        | gag<br>Glu        | atg<br>Met        | cag<br>Gln<br>320 | gaa<br>Glu          | ggc<br>Gly            | cac<br>His        | ggc<br>Gly            | ggc<br>Gly<br>325 | tgg<br>Trp          | aac<br>Asn            | 1073 |
| Pro                   | agg<br>Arg                 | atg<br>Met<br>330  | Ala                        | gag<br>Glu          | ttt<br>Phe        | atc<br>Ile        | gga<br>Gly<br>335 | cag<br>Gln        | acg<br>Thr          | ggc<br>Gly            | acc<br>Thr        | gtg<br>Val<br>340     | cat<br>His        | cgt<br>Arg          | atc<br>lle            | 1121 |
| acg<br>Thr            | gac<br>Asp<br>345          | cgc<br>Arg         | ggg<br>Gly                 | gac<br>Asp          | gtg<br>Val        | cgc<br>Arg<br>350 | gtg<br>Val        | cag<br>G n        | ttc<br>Phe          | aac<br>Asn            | cac<br>His<br>355 | Glu                   | acg<br>Thr        | cgc<br>Arg          | tgg<br>Trp            | 1169 |
| acc<br>Thr<br>360     | ttc<br>Phe                 | cac<br>His         | ccc<br>Pro                 | ggg<br>Gly          | gcg<br>Ala<br>365 | ctc<br>Leu        | acc<br>Thr        | aag<br>Lys        | cac<br>His          | cac<br>His<br>370     | tcc<br>Ser        | ttc<br>Phe            | tgg<br>Trp        | gtg<br>Val          | ggc<br>Gly<br>375     | 1217 |
| gac<br>Asp            | gtg<br>Val                 | gtc<br>Val         | cgg<br>Arg                 | gtc<br>Val<br>380   | atc<br>He         | ggc<br>Gly        | gac<br>Asp        | ctt<br>Leu        | gac<br>Asp<br>385   | aca<br>Thr            | gtg<br>Val        | aag<br>Lys            | cgg<br>Arg        | ctg<br>Leu<br>390   | cag<br>Gln            | 1265 |
| gct<br>Ala            | ggg<br>Gly                 | cat<br>His         | ggc<br>Gly<br>395          | gag<br>Glu          | tgg<br>Trp        | acg<br>Thr        | Asp               | gac<br>Asp<br>400 | atg<br>Met          | gcc<br>Ala            | cct<br>Pro        | gcc<br>Ala            | ctg<br>Leu<br>405 | ggc<br>Gly          | cgc<br>Arg            | 1313 |
| gtc<br>Val            | ggg<br>Gly                 | aag<br>Lys<br>410  | gtg<br>Val                 | gtg<br>Val          | aaa<br>Lys        | Val               | ttt<br>Phe<br>415 | gga<br>Gly        | gac<br>Asp          | ggg<br>Gly            | aac<br>Asn        | ctg<br>Leu<br>420     | cgt<br>Arg        | gta<br>Val          | gca<br>Ala            | 1361 |
| gtc<br>Val            | gct<br>Ala                 | ggt<br>Gly         | cag<br>Gin                 | cgg<br>Arg          | tgg<br>Trp        | acc<br>Thr        | ttc<br>Phe        | agc<br>Ser        | ccc<br>Pro          | tcc<br>Ser            | tgc<br>Cys        | ctg<br>Leu            | gtg<br>Val        | gcc<br>Ala          | tac<br>Tyr            | 1409 |

|                       |                   |                   |                            |                     | _                     |                           |                    |                           |                                 |                    |                    |                           | •                         |                    |                       |      |
|-----------------------|-------------------|-------------------|----------------------------|---------------------|-----------------------|---------------------------|--------------------|---------------------------|---------------------------------|--------------------|--------------------|---------------------------|---------------------------|--------------------|-----------------------|------|
| cg<br>Ar<br>44        | gr                | c ga              | ag ga<br>Iu Gl             | ag ga<br>Lu As      | at go<br>sp Al<br>44  | a As                      | ic ct<br>in Le     | g ga<br>u As <sub>l</sub> | c gt<br>o Va                    | g gc<br>I Al<br>45 | a Gl               | g cg<br>u Ar              | c gc<br>g Al              | с сg<br>a Ar       | g gag<br>g Glu<br>455 | 1457 |
| aa<br>As              | c aa<br>n Ly      | a ag<br>s Se      | go to<br>er Se             | a ct<br>er Le<br>46 | eu Se                 | gc gt<br>er Va            | g gc<br>I Ai       | c ct;<br>a Lei            | g ga<br>u As <sub>l</sub><br>46 | p Ly:              | g ct<br>s Le       | t cg<br>u Ar              | g gc<br>g Al              | c ca<br>a Gl<br>47 | g aag<br>n Lys<br>O   | 1505 |
| ag <sup>.</sup><br>Se | t ga<br>r As      | c cc<br>p Pr      | a ga<br>o Gl<br>47         | u Hi                | s Pr                  | g gg<br>o Gl              | a ag<br>y Ar       | g ctg<br>g Lei<br>480     | ı Va                            | g gtø<br>I Va      | g ga<br>  Gl       | g gt <sub>i</sub><br>u Va | g gc<br>  A <br> <br>  48 | a Le               | g ggt<br>u Gly        | 1553 |
| aad<br>Asr            | c goa<br>n Ala    | agc<br>aAl<br>49  | a Ar                       | g gc<br>g Al        | t ct<br>a Le          | g ga<br>u As <sub>l</sub> | c ct<br>b Le<br>49 | u Lei                     | g cgg<br>ı Arg                  | g agg<br>g Arg     | g cgo<br>g Ar      | c cca<br>g Pro<br>500     | o Glo                     | g ca<br>u Gl       | a gtg<br>n Val        | 1601 |
| gac<br>Asp            | aco<br>Thi<br>505 | ' Ly              | g aa<br>s As               | c ca<br>n Gl        | a gg<br>n Gl          | c agg<br>y Arg<br>51(     | g Ih               | c gct<br>r Ala            | ctg<br>Leu                      | g caa<br>u Glr     | agtg<br>val<br>515 | l Ala                     | gco<br>Ala                | c tad              | c ctg<br>Leu          | 1649 |
| ggo<br>Gly<br>520     | GIT               | g gt<br>n Va      | g ga <sub>l</sub><br>I Gli | g tt;<br>u Lei      | g ata<br>u 11a<br>528 | e Arg                     | g ctg<br>g Lei     | g ctg<br>I Leu            | cta<br>Leu                      | caa<br>Gln<br>530  | ı Ala              | c agg<br>a Arg            | g gcg<br>Ala              | g ggo<br>Gly       | gtg<br>Val<br>535     | 1697 |
| gac<br>Asp            | ctg<br>Leu        | Pro               | g gad<br>o Asp             | gad<br>Asp<br>540   | o Glu                 | g ggo<br>u Gly            | aad<br>Asr         | acg<br>Thr                | gca<br>Ala<br>545               | Leu                | cac<br>His         | tac<br>Tyr                | gcg<br>Ala                | gcc<br>Ala<br>550  | ctg<br>Leu            | 1745 |
| ggg<br>Gly            | aac<br>Asn        | cag<br>Gir        | 9 ccc<br>9 Pro<br>555      | ) GIL               | g gcc<br>ı Ala        | acc<br>Thr                | agg<br>Arg         | gtg<br>Val<br>560         | ctc<br>Leu                      | ctg<br>Leu         | agt<br>Ser         | gct<br>Ala                | ggg<br>Gly<br>565         | tgc<br>Cys         | cgg<br>Arg            | 1793 |
| gcg<br>Ala            | gac<br>Asp        | gcc<br>Ala<br>570 | He                         | aac<br>Asn          | ago<br>Ser            | acc<br>Thr                | cag<br>Gln<br>575  | agc<br>Ser                | aca<br>Thr                      | gca<br>Ala         | ctg<br>Leu         | cac<br>His<br>580         | gtg<br>Val                | gcc<br>Ala         | gtg<br>Val            | 1841 |
| cag<br>Gln            | agg<br>Arg<br>585 | ggc<br>Gly        | ttc<br>Phe                 | ctg<br>Leu          | gag<br>Glu            | gtg<br>Val<br>590         | gtg<br>Val         | cgg<br>Arg                | gcc<br>Ala                      | ctg<br>Leu         | tgt<br>Cys<br>595  | gag<br>Glu                | cgc<br>Arg                | ggc<br>Gly         | tgt<br>Cys            | 1889 |
| gac<br>Asp<br>600     | gtc<br>Val        | aac<br>Asn        | ctg<br>Leu                 | ccc<br>Pro          | gac<br>Asp<br>605     | gcc<br>Ala                | cac<br>His         | tcg<br>Ser                | gac<br>Asp                      | acg<br>Thr<br>610  | ccc<br>Pro         | ctg<br>Leu                | cac<br>His                | tcc<br>Ser         | gcc<br>Ala<br>615     | 1937 |
| atc<br>lle            | tcg<br>Ser        | gcg<br>Ala        | ggc<br>Gly                 | act<br>Thr<br>620   | gga<br>Gly            | gcc<br>Ala                | agc<br>Ser         | ggc<br>Gly                | att<br>He<br>625                | gtc<br>Val         | gag<br>Glu         | gtc<br>Val                | ctc<br>Leu                | acg<br>Thr<br>630  | gag<br>Glu            | 1985 |
| gtg<br>Val            | cca<br>Pro        | aac<br>Asn        | atc<br>lle<br>635          | gat<br>Asp          | gtt<br>Val            | acc<br>Thr                | gcc<br>Ala         | acc<br>Thr<br>640         | aac<br>Asn                      | agc<br>Ser         | cag<br>Gln         | Gly                       | ttc<br>Phe<br>645         | acc<br>Thr         | ctg<br>Leu            | 2033 |
| ctg<br>Leu            | HIS               | cat<br>His<br>650 | gcc<br>Ala                 | tcc<br>Ser          | ctc<br>Leu            | aag<br>Lys                | ggt<br>Gly<br>655  | cac .<br>His .            | gcg<br>Ala                      | cta<br>Leu         | gct<br>Ala         | gtg<br>Val<br>660         | aga<br>Arg                | aag<br>Lys         | att<br>He             | 2081 |

| ctg<br>Leu | gct<br>Ala<br>665 | Arg               | gcg<br>Ala | cgg<br>Arg        | g<br>G l n        | ctg<br>Leu<br>670 | gtg<br>Val        | gac<br>Asp | gcc<br>Ala        | aag<br>Lys | aag<br>Lys<br>675 | gag<br>Glu        | g<br>Asp   | ggc<br>Gly        | ttc<br>Phe | 2129 |
|------------|-------------------|-------------------|------------|-------------------|-------------------|-------------------|-------------------|------------|-------------------|------------|-------------------|-------------------|------------|-------------------|------------|------|
|            | Ala               |                   |            |                   | gct<br>Ala<br>685 |                   |                   |            |                   |            |                   |                   |            |                   |            | 2177 |
| atc<br>Ile | ctc<br>Leu        | atc<br>lle        | cgg<br>Arg | gag<br>Glu<br>700 | ggc<br>Gly        | cgc<br>Arg        | tgt<br>Cys        | gac<br>Asp | gtg<br>Val<br>705 | aac<br>Asn | gtg<br>Val        | cgc<br>Arg        | aac<br>Asn | cgg<br>Arg<br>710 | aag<br>Lys | 2225 |
|            |                   |                   |            |                   | cat<br>His        |                   |                   |            |                   |            |                   |                   |            |                   |            | 2273 |
| gtg<br>Val | ccg<br>Pro        | cta<br>Leu<br>730 | ctg<br>Leu | gtg<br>Val        | gac<br>Asp        | gct<br>Ala        | ggg<br>Gly<br>735 | tgc<br>Cys | agt<br>Ser        | gtc<br>Val | aac<br>Asn        | gcc<br>Ala<br>740 | gag<br>Glu | gac<br>Asp        | gag<br>Glu | 2321 |
|            |                   |                   |            |                   | ctg<br>Leu        |                   |                   |            |                   |            |                   |                   |            |                   |            | 2369 |
|            |                   |                   |            |                   | ggg<br>Gly<br>765 |                   |                   |            |                   |            |                   |                   |            |                   |            | 2417 |
|            |                   |                   |            |                   | gcc<br>Ala        |                   |                   |            |                   |            |                   |                   |            |                   |            | 2465 |
|            |                   |                   |            |                   | gcc<br>Ala        |                   |                   |            |                   |            |                   |                   |            |                   |            | 2513 |
| agc<br>Ser | tac<br>Tyr        | Thr               | Asn        | His               | cgc<br>Arg        | Gly               | Arg               | Ser        | Pro               | Leu        | Asp               | Leu               | Ala        | gcc<br>Ala        | gag<br>Glu | 2561 |
| ggt<br>G∣y | cgc<br>Arg<br>825 | gtg<br>Val        | ctc<br>Leu | aag<br>Lys        | gcc<br>Ala        | ctt<br>Leu<br>830 | cag<br>Gln        | ggc<br>Gly | tgc<br>Cys        | gcc<br>Ala | cag<br>Gln<br>835 | cgc<br>Arg        | ttc<br>Phe | cgg<br>Arg        | gag<br>Glu | 2609 |
|            |                   |                   |            |                   | ggc<br>Gly<br>845 |                   |                   |            |                   |            |                   |                   |            |                   |            | 2657 |
|            |                   |                   |            |                   | acg<br>Thr        |                   |                   |            |                   |            |                   |                   |            |                   |            | 2705 |
|            |                   | Ala               |            |                   | ctg<br>Leu        |                   | Cys               |            |                   |            |                   |                   |            |                   |            | 2753 |
|            |                   |                   |            |                   | cac<br>His        |                   |                   |            |                   |            |                   |                   |            |                   |            | 2801 |

|  |                       |                   | `                 |                   |                   | 000               |                   |                   |                   |                   | 300               |                   |                   |                   |      |
|--|-----------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| atg aa<br>Met Ly<br>90   | /s Lys                | tgc<br>Cys        | atc<br>  e        | agg<br>Arg        | tgc<br>Cys<br>910 | Gln               | gtg<br>Val        | gtc<br>Val        | gtc<br>Val        | agc<br>Ser<br>915 | Lys               | aaa<br>Lys        | ctg<br>Leu        | cgc<br>Arg        | 2849 |
| cca ga<br>Pro As<br>920  | oc ggc<br>op Gly      | tct<br>Ser        | gag<br>Glu        | gtg<br>Val<br>925 | gcg<br>Ala        | agc<br>Ser        | gcc<br>Ala        | gcc<br>Ala        | ccc<br>Pro<br>930 | Ala               | ccc<br>Pro        | ggc<br>Gly        | ccg<br>Pro        | ccg<br>Pro<br>935 | 2897 |
| cgc ca<br>Arg Gl   | ng ctg<br>n Leu       | gtg<br>Val        | gag<br>Glu<br>940 | Glu               | ctg<br>Leu        | cag<br>Gln        | agc<br>Ser        | cgc<br>Arg<br>945 | tac<br>Tyr        | cgg<br>Arg        | cag<br>Gln        | atg<br>Met        | gag<br>Glu<br>950 | Glu               | 2945 |
| cgc at<br>Arg li   | c acc<br>e Thr        | tgc<br>Cys<br>955 | ccc<br>Pro        | atc<br>lle        | tgc<br>Cys        | atc<br>Ile        | gac<br>Asp<br>960 | agc<br>Ser        | cac<br>His        | atc<br>Ile        | cgc<br>Arg        | ctc<br>Leu<br>965 | Val               | ttc<br>Phe        | 2993 |
| cag tg<br>Gln Cy   | c ggc<br>s Gly<br>970 | cac<br>His        | ggc<br>Gly        | gca<br>Ala        | tgc<br>Cys        | gcc<br>Ala<br>975 | ccc<br>Pro        | tgc<br>Cys        | ggc<br>Gly        | tcc<br>Ser        | gcg<br>Ala<br>980 | ctc<br>Leu        | agc<br>Ser        | gcc<br>Ala        | 3041 |
| tgc cc<br>Cys Pr<br>98   | o He                  | tgc<br>Cys        | cgc<br>Arg        | cag<br>Gln        | ccc<br>Pro<br>990 | atc<br>Ile        | cgc<br>Arg        | gac<br>Asp        | cgc<br>Arg        | atc<br>Ile<br>995 | cag<br>G n        | atc<br>He         | ttc<br>Phe        | gtg<br>Val        | 3089 |
| tgagcc   | gcgc                  | egte              | gcc               | gc go             | ccg               | agct              | g cc              | ttcg              | cgtg              | ccc               | ccgc              | cct               | gtgt              | tttata            | 3149 |
| aaaaga   | aaga                  | ttct              | gga               | t                 |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | 3168 |
| <210><br><211> (212> (213> (213> (213) (213) (213) (213) (213) (213) (213) (213) | 999<br>PRT            | sap i e           | ens               |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |      |
| <400>  |                       |                   | 5                 | •                 |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |      |
| Met Gly  | y Irp                 | Lys               | Pro<br>5          | Ser               | Glu               | Ala               | Arg               | 10                | Gln               | Ser               | Gln               | Ser               | Leu<br>15         | Gln               |      |
| Ala Se   | r Gly                 | Leu<br>20         | Gln               | Pro               | Arg               | Ser               | Leu<br>25         | Lys               | Ala               | Ala               | Arg               | Arg<br>30         | Ala               | Thr               |      |
| Gly Ar   | g Pro<br>35           | Asp               | Arg               | Ser               | Arg               | Ala<br>40         | Ala               | Pro               | Pro               | Asn               | Met<br>45         | Asp               | Pro               | Asp               |      |
| Pro Gla  | n Ala                 | Glv               | Val               | Gln               | Val               | Gly               | Met               | Arg               | Val               | Val               | Arg               | Gly               | Val               | Asp               |      |
| 50   | )                     | ,                 |                   |                   | 55                |                   |                   |                   |                   | 60                |                   |                   |                   | ·                 |      |
| Trp Lys  | )                     |                   |                   |                   | 55                |                   |                   |                   | Gly<br>75         |                   | Val               | Gly               | Thr               |                   |      |

Val Val Gln Trp Asp Gln Gly Thr Arg Thr Asn Tyr Arg Ala Gly Tyr 100 105 110

- Arg His Pro Asn IIe IIe Cys Asp Cys Cys Lys Lys His Gly Leu Arg 130 135 140
- Gly Met Arg Trp Lys Cys Arg Val Cys Leu Asp Tyr Asp Leu Cys Thr 145 150 155 160
- Gln Cys Tyr Met His Asn Lys His Glu Leu Ala His Ala Phe Asp Arg 165 170 175
- Tyr Glu Thr Ala His Ser Arg Pro Val Thr Leu Ser Pro Arg Gln Gly 180 185 190
- Leu Pro Arg Ile Pro Leu Arg Gly Ile Phe Gln Gly Ala Lys Val 195 200 205
- Arg Gly Pro Phe Trp Glu Trp Gly Ser Gln Asp Gly Gly Glu Gly Lys 210 220
- Pro Gly Arg Val Val Asp Ile Arg Gly Trp Asp Val Glu Thr Gly Arg 225 230 235 240
- Ser Val Ala Ser Val Thr Trp Ala Asp Gly Thr Thr Asn Val Tyr Arg 245 250 255
- Val Gly His Lys Gly Lys Val Asp Leu Lys Cys Val Gly Glu Ala Ala 260 270
- Gly Gly Phe Tyr Tyr Lys Asp His Leu Pro Arg Leu Gly Lys Pro Ala 275 280 285
- Glu Leu Gin Arg Arg Val Ser Ala Asp Ser Gin Pro Phe Gin His Gly 290 295 300
- Asp Lys Val Lys Cys Leu Leu Asp Thr Asp Val Leu Arg Glu Met Gln 305 310 315 320
- Glu Gly His Gly Gly Trp Asn Pro Arg Met Ala Glu Phe Ile Gly Gln 325 330 335
- Thr Gly Thr Val His Arg Ile Thr Asp Arg Gly Asp Val Arg Val Gln 340 350
- Phe Asn His Glu Thr Arg Trp Thr Phe His Pro Gly Ala Leu Thr Lys 355 360 365
- His His Ser Phe Trp Val Gly Asp Val Val Arg Val Ile Gly Asp Leu 370 380
- Asp Thr Val Lys Arg Leu Gln Ala Gly His Gly Glu Trp Thr Asp Asp 385 390 395 400
- Met Ala Pro Ala Leu Gly Arg Val Gly Lys Val Val Lys Val Phe Gly 405 410 415
- Asp Gly Asn Leu Arg Val Ala Val Ala Gly Gln Arg Trp Thr Phe Ser

Pro Ser Cys Leu Val Ala Tyr Arg Pro Glu Glu Asp Ala Asn Leu Asp 435 440 Val Ala Glu Arg Ala Arg Glu Asn Lys Ser Ser Leu Ser Val Ala Leu 450 Asp Lys Leu Arg Ala Gln Lys Ser Asp Pro Glu His Pro Gly Arg Leu Val Val Glu Val Ala Leu Gly Asn Ala Ala Arg Ala Leu Asp Leu Leu Arg Arg Pro Glu Gln Val Asp Thr Lys Asn Gln Gly Arg Thr Ala Leu Gin Val Ala Ala Tyr Leu Gly Gin Val Glu Leu ile Arg Leu Leu Leu Gin Ala Arg Ala Giy Val Asp Leu Pro Asp Asp Giu Giy Asn Thr 540 Ala Leu His Tyr Ala Ala Leu Gly Asn Gln Pro Glu Ala Thr Arg Val Leu Leu Ser Ala Gly Cys Arg Ala Asp Ala lle Asn Ser Thr Gln Ser 570 Thr Ala Leu His Val Ala Val Gln Arg Gly Phe Leu Glu Val Val Arg 585 Ala Leu Cys Glu Arg Gly Cys Asp Val Asn Leu Pro Asp Ala His Ser Asp Thr Pro Leu His Ser Ala Ile Ser Ala Gly Thr Gly Ala Ser Gly 610 615 lle Val Glu Val Leu Thr Glu Val Pro Asn lle Asp Val Thr Ala Thr Asn Ser Gln Gly Phe Thr Leu Leu His His Ala Ser Leu Lys Gly His Ala Leu Ala Val Arg Lys lle Leu Ala Arg Ala Arg Gln Leu Val Asp Ala Lys Lys Glu Asp Gly Phe Thr Ala Leu His Leu Ala Ala Leu Asn Asn His Arg Glu Val Ala Gln Ile Leu Ile Arg Glu Gly Arg Cys Asp Val Asn Val Arg Asn Arg Lys Leu Gln Ser Pro Leu His Leu Ala Val 705

730

Gln Gln Ala His Val Gly Leu Val Pro Leu Leu Val Asp Ala Gly Cys

725

Ser Val Asn Ala Glu Asp Glu Glu Gly Asp Thr Ala Leu His Val Ala 740 745 750

Leu Gln Arg His Gln Leu Leu Pro Leu Val Ala Asp Gly Ala Gly Gly 755 760 765

Asp Pro Gly Pro Leu Gln Leu Leu Ser Arg Leu Gln Ala Ser Gly Leu 770 780

Pro Gly Ser Ala Glu Leu Thr Val Gly Ala Ala Val Ala Cys Phe Leu 785 790 795 800

Ala Leu Glu Gly Ala Asp Val Ser Tyr Thr Asn His Arg Gly Arg Ser 805 810 815

Pro Leu Asp Leu Ala Ala Glu Gly Arg Val Leu Lys Ala Leu Gln Gly 820 830

Cys Ala Gin Arg Phe Arg Glu Arg Gin Ala Giy Giy Ala Ala Pro 835 840 845

Gly Pro Arg Gln Thr Leu Gly Thr Pro Asn Thr Val Thr Asn Leu His 850 860

Val Gly Ala Ala Pro Gly Pro Glu Ala Ala Glu Cys Leu Val Cys Ser 865 870 875 880

Glu Leu Ala Leu Leu Val Leu Phe Ser Pro Cys Gln His Arg Thr Val 885 890 895

Cys Glu Glu Cys Ala Arg Arg Met Lys Lys Cys Ile Arg Cys Gln Val 900 910

Val Val Ser Lys Leu Arg Pro Asp Gly Ser Glu Val Ala Ser Ala 915 920 925

Ala Pro Ala Pro Gly Pro Pro Arg Gln Leu Val Glu Glu Leu Gln Ser 930 935 940

Arg Tyr Arg Gln Met Glu Glu Arg Ile Thr Cys Pro Ile Cys Ile Asp 945 950 955 960

Ser His Ile Arg Leu Val Phe Gln Cys Gly His Gly Ala Cys Ala Pro 965 970 975

Cys Gly Ser Ala Leu Ser Ala Cys Pro Ile Cys Arg Gln Pro Ile Arg 980 985 990

Asp Arg Ile Gln Ile Phe Val 995

<210> 163

<211> 4031

<212> DNA

<213> Homo sapiens

| <220><br><221> CDS<br><222> (91) (264)          | 9)  |   |   |
|---|---|---|---|
| <400> 163                                       | agata atagaagata                            |   |   |
|   |   |   | egcgc ccggtcgccg 60                         |
| tooogtogoo aatoo                                | cegee greeegggee                            | atg atc gcc tgg<br>Met IIe Ala Trp<br>1         | cgt ctg ccc ttg 114<br>Arg Leu Pro Leu<br>5 |
| tgc gtg ctc ttg g<br>Cys Val Leu Leu \<br>10    | gtg gcc tcc gtc<br>/al Ala Ser Val<br>15    | gag agc cac ctg g<br>Glu Ser His Leu G<br>20    | gg gcc ctg ggg 162<br>ly Ala Leu Gly        |
| ccc aag aac gtc t<br>Pro Lys Asn Val S<br>25    | cg cag aaa gac<br>er GIn Lys Asp<br>30      | gcg gag ttt gag c<br>Ala Glu Phe Glu A<br>35    | gc acc tac gcg 210<br>rg Thr Tyr Ala<br>40  |
| gac gac gtc aac a<br>Asp Asp Val Asn S          | gc gag ctg gtc<br>er Glu Leu Val<br>45      | aac atc tac acc t<br>Asn lle Tyr Thr Pl<br>50   | tc aac cac acc 258<br>ne Asn His Thr<br>55  |
| gtg acc cgc aac c<br>Val Thr Arg Asn A<br>60    | gg acc gag ggt g<br>rg Thr Glu Gly V        | gtg cga gtg tct g<br>/al Arg Val Ser Va<br>65   | tg aat gtc ctg 306<br>al Asn Val Leu<br>70  |
| aac aag cag aaa g<br>Asn Lys GIn Lys G<br>75    | gg gcg cct ttg o<br>ly Ala Pro Leu L<br>80  | eu Phe Val Val Ar.                              | gc cag aag gag 354<br>gg Gln Lys Glu<br>35  |
| gct gtt gtg tcc t<br>Ala Val Val Ser Pl<br>90   | to cag gtg ccc c<br>ne Gln Val Pro L<br>95  | ta atc ctt cga gg<br>eu lle Leu Arg Gl<br>100   | a ctg tat cag 402<br>y Leu Tyr GIn          |
| cgg aag tac ctc ta<br>Arg Lys Tyr Leu Ty<br>105 | ac caa aaa gtg g<br>yr Gln Lys Val G<br>110 | aa cga act ctg tg<br>Iu Arg Thr Leu Cy<br>115   | t cag ccc ccc 450<br>s Gln Pro Pro<br>120   |
| acc aag aat gag to<br>Thr Lys Asn Glu Se<br>12  | r Glu lle Gin P                             | tt ttc tat gtg ga<br>he Phe Tyr Vai As<br>130   | c gtg tct acc 498<br>p Val Ser Thr<br>135   |
| ctg tca ccc gtc aa<br>Leu Ser Pro Val As<br>140 | n ihr ihr lyr G                             | ag ctc cga gtc aa<br>In Leu Arg Val As<br>45    | c cgt gtg gac 546<br>n Arg Val Asp<br>150   |
| aat ttt gtg ctc ag<br>Asn Phe Val Leu Ar<br>155 | g act gga gag c<br>g Thr Gly Glu Lo<br>160  | tg ttt acc ttt aa<br>eu Phe Thr Phe Asi<br>169  | n Thr Thr Ala                               |
| gcc cag ccc cag ta<br>Ala Gln Pro Gln Ty<br>170 | c ttc aaa tac ga<br>r Phe Lys Tyr G<br>175  | ag ttt cct gat ggi<br>Iu Phe Pro Asp Gly<br>180 | t gtg gac tcg 642<br>Val Asp Ser            |
| gta att gtc aag gt;<br>Val lle Val Lys Va       | g acc tcc aag aa<br>I Thr Ser Lys Ly        | ag gcc ttc ccc tgc<br>vs Ala Phe Pro Cys        | c tca gtc atc 690<br>s Ser Val IIe          |

| tcc<br>Ser                     | atc (<br>lle (     | cag g<br>Gln A            | (SP)                 | stc o<br>al L<br>05  | tg t<br>eu C          | gc d<br>ys F       | cct<br>Pro     | gto<br>Val        | ta<br>Ty<br>21    | r A               | at c<br>sp L      | tg (<br>.eu /      | gac<br>Asp         | aac<br>Asn         | ag<br>Se<br>21    | t gta<br>r Val    | 738  |
|--------------------------------|--------------------|---------------------------|----------------------|----------------------|-----------------------|--------------------|----------------|-------------------|-------------------|-------------------|-------------------|--------------------|--------------------|--------------------|-------------------|-------------------|------|
| gcc i<br>Ala F                 | ttc a<br>Phe l     | 100                       | gc a<br>Hy M<br>220  | tg t<br>et T         | ac c<br>yr G          | ag a<br>In T       | nr             | atg<br>Met<br>225 | In                | t aa<br>r Ly      | ag a<br>ys L      | ag g<br>ys A       | Na A               | gcc<br>Ala<br>230  | ato               | act<br>Thr        | 786  |
| gtg o<br>Val (                 |                    | gg a<br>rg L<br>35        | aa g<br>ys A         | ac t<br>sp P         | tc c<br>he P          | ro s               | gc<br>er<br>40 | aac<br>Asn        | ago<br>Sei        | c ti<br>r Pł      | tc t<br>ne T      | yr V               | tg g<br>al V<br>45 | gtg<br>/al         | gtg<br>Val        | gta<br>Val        | 834  |
| gtg a<br>Val L<br>2            | ag a<br>ys T<br>50 | ct g<br>hr G              | ag g<br>lu A         | ac c<br>sp G         | ag go<br>In A<br>25   | ia U               | gc (<br>ys (   | gga<br>Gly        | gge<br>Gly        | g to<br>/ Se      | r Le              | tg c<br>eu P<br>80 | cc t<br>ro P       | tc<br>he           | tac<br>Tyr        | cct<br>Pro        | 882  |
| ttt g<br>Phe V<br>265          | tg ga<br>al G      | aa ga<br>lu As            | at ga<br>sp G        | ag co<br>lu Pi<br>27 | 0 45                  | g ga               | at d<br>sp (   | aa<br>In          | ggg<br>Gly        | ca<br>Hi<br>27    | s Ar              | gt ca              | ag a<br>In L       | aa<br>ys           | aca<br>Thr        | ctg<br>Leu<br>280 | 930  |
| tca g<br>Ser V                 | tg ct<br>al Le     | ig gt<br>eu Va            | to to<br>al Se<br>28 | , ui                 | ng go<br>n Al         | t gt<br>a Va       | c a            | nr                | tct<br>Ser<br>290 | GII               | g go<br>u Al      | c ta<br>a Ty       | at g<br>/r Va      | ai (               | ggt<br>Gly<br>295 | ggg<br>Gly        | 978  |
| atg ct<br>Met Le               | tc tt<br>eu Ph     | t tg<br>e Cy<br>30        | 3 LE                 | g gg<br>u Gl         | c at<br>y li          | a tt<br>e Ph       | e L            | tg<br>eu<br>05    | tcc<br>Ser        | tto<br>Phe        | c ta<br>e Ty      | c ct<br>r Le       | g ct<br>u Le<br>31 | eu T               | act<br>hr         | gtg<br>Val        | 1026 |
| ctg ct<br>Leu Le               | g gc<br>u Al<br>31 | ч Оу                      | t tg<br>s Tr         | g ga<br>p Gl         | g aa<br>u Asi         | c tg<br>n Tr<br>32 | ра             | gg (<br>rg (      | caa<br>Gln        | agg<br>Arg        | g aag<br>Lys      | g aa<br>s Ly<br>32 | s Th               | c t<br>r L         | tg<br>eu          | ctg<br>Leu        | 1074 |
| gtg gc<br>Val Al<br>33         | ~                  | a ga<br>e As <sub>l</sub> | c cga<br>p Ara       | a gco<br>g Ala       | c tgo<br>a Cys<br>335 | Fre                | a ga<br>o Gl   | aa a<br>u S       | agt<br>Ser        | ggt<br>Gly        | cac<br>His        | A la               | t cg<br>a Ar       | g g<br>g V         | tc<br>al          | ttg<br>Leu        | 1122 |
| gct ga<br>Ala As<br>345        | t toa<br>p Ser     | tti<br>Phe                | t cct<br>e Pro       | ggo<br>Gly<br>350    | ser                   | gco<br>Ala         | c cc<br>a Pr   | t t<br>o T        | yr                | gag<br>Glu<br>355 | ggt<br>Gly        | tad<br>Tyr         | c aa<br>r Asi      | c ta<br>n Ty       | yr (              | ggc<br>Gly<br>360 | 1170 |
| tcc tt <sup>-</sup><br>Ser Phe | t gaa<br>e Glu     | aat<br>Asr                | ggt<br>Gly<br>365    | 361                  | gga<br>Gly            | tcc<br>Ser         | ac<br>Th       | r A               | ac<br>sp<br>70    | ggg<br>Gly        | ttg<br>Leu        | gtt<br>Val         | gaa<br>Glu         | a ag<br>u Se<br>37 | er /              | gca<br>Na         | 1218 |
| ggt toa<br>Gly Ser             | a ggg<br>Gly       | gac<br>Asp<br>380         | LCu                  | tcc<br>Ser           | tac<br>Tyr            | agt<br>Ser         | ta<br>Ty<br>38 | r G               | ag į<br>In (      | ggg<br>Gly        | cac<br>His        | gac<br>Asp         | cag<br>Glr<br>390  | ı Ph               | ic a<br>ne L      | ag<br>ys          | 1266 |
| cgg cgc<br>Arg Arg             | ctt<br>Leu<br>395  | ccc<br>Pro                | tct<br>Ser           | ggc<br>Gly           | cag<br>Gln            | atg<br>Met<br>400  | cg;<br>Arį     | g ca<br>g G       | ag d<br>In L      | ctg<br>_eu        | tgc<br>Cys        | att<br>Ile<br>405  | gcc<br>Ala         | at<br>Me           | g g<br>t A        | ac<br>sp          | 1314 |
| cgc tcc<br>Arg Ser<br>410      | , ,,,              | gac<br>Asp                | gca<br>Ala           | gtg<br>Val           | ggt<br>Gly<br>415     | cct<br>Pro         | cgg<br>Arg     | g co<br>g Pr      | ct c<br>ro A      | ۱rg               | ctg<br>Leu<br>420 | gac<br>Asp         | tcc<br>Ser         | at<br>Me           | g a<br>t S        | gc<br>er          | 1362 |

| tcc gtg g<br>Ser Val G<br>425     | aa gag ga<br>lu Glu As                   | at c ta<br>sp Asp Ty<br>430   | c gac a<br>r Asp T         | nr Leu I                    | act gac at<br>Thr Asp II<br>135 | c getca gad<br>e Asp Ser Asp<br>440   | ס      |
|-----------------------------------|--|-------------------------------|----------------------------|-----------------------------|---------------------------------|---------------------------------------|--------|
| aaa aac g<br>Lys Asn V            | tc att cg<br>al lle Ar<br>44             | g iiii Ly:                    | g caa ta<br>s Gln Ty       | ac ctc t<br>yr Leu 0<br>450 | gt gtg gc<br>Cys Val Ala        | t gat ctg gca<br>a Asp Leu Ala<br>455 | a 1458 |
| cga aag ga<br>Arg Lys As          | ac aaa cg<br>sp Lys Ar<br>460            | t gtt ttg<br>g Va! Lei        | g cgg aa<br>u Arg Ly<br>46 | /S Lys I                    | ac cag att<br>yr Gln lle        | t tac ttc tgg<br>F Tyr Phe Trp<br>470 | 1506   |
| aac ata go<br>Asn Ile Al<br>47    | ω 11/1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 | t gcg gto<br>e Ala Val        | ttc ta<br>Phe Ty<br>480    | ec gca c<br>r Ala L         | tt cct gtg<br>eu Pro Val<br>485 | gtg cag ctg<br>Val Gin Leu            | 1554   |
| gtg atc ac<br>Val IIe Th<br>490   | c tac cap<br>r Tyr Gli                   | g acg gtg<br>n Thr Val<br>495 | Val AS                     | t gtc ad<br>n Val Th        | ca ggg aac<br>hr Gly Asn<br>500 | cag gac atc<br>Gln Asp lle            | 1602   |
| tgc tac ta<br>Cys Tyr Ty<br>505   | c aac tto<br>r Asn Phe                   | ctc tgt<br>Leu Cys<br>510     | gcc ca<br>Ala Hi           | c ccg ct<br>s Pro Le<br>51  | eu Gly Asn                      | ctc agc gcc<br>Leu Ser Ala<br>520     | 1650   |
| ttc aac aa<br>Phe Asn As          | c atc cto<br>n lle Leu<br>525            | Sei ASII                      | ttg ggg<br>Leu Gly         | g tac at<br>y Tyr II<br>530 | c ctg ctg<br>e Leu Leu          | ggg ctg ctc<br>Gly Leu Leu<br>535     | 1698   |
| ttc ctg ctc<br>Phe Leu Lei        | atc atc<br>Ile Ile<br>540                | ctg cag<br>Leu Gln            | cga gag<br>Arg Glu<br>545  | ı Ile As                    | t cat aac<br>n His Asn          | cgg gcc ctg<br>Arg Ala Leu<br>550     | 1746   |
| ctg cgg aat<br>Leu Arg Asr<br>555 | Map Leu                                  | tat gct<br>Tyr Ala            | ctg gag<br>Leu Glu<br>560  | tgt ggg<br>Cys Gly          | g atc ccc<br>y lle Pro<br>565   | aaa cac ttt<br>Lys His Phe            | 1794   |
| ggt ctg ttt<br>Gly Leu Phe<br>570 | tac gcc<br>Tyr Ala                       | atg ggc<br>Met Gly<br>575     | aca gca<br>Thr Ala         | ctg atg<br>Leu Met          | g atg gag<br>t Met Glu<br>580   | ggg cta ctt<br>Gly Leu Leu            | 1842   |
| agt gcc tgt<br>Ser Ala Cys<br>585 | tac cac<br>Tyr His                       | gtc tgc<br>Val Cys<br>590     | ccc aac<br>Pro Asn         | tac acc<br>Tyr Thr<br>595   | Asn Phe (                       | cag ttt gat<br>Gln Phe Asp<br>600     | 1890   |
| acc tcc ttc<br>Thr Ser Phe        | atg tac<br>Met Tyr<br>605                | atg att ø<br>Met lle /        | gct ggc<br>Ala Gly         | ctc tgc<br>Leu Cys<br>610   | atg ctg a<br>Met Leu L          | aag ctc tac<br>ys Leu Tyr<br>615      | 1938   |
| cag aag cgg<br>GIn Lys Arg        | cac cca<br>His Pro<br>620                | gat atc a<br>Asp lle A        | aac gcc<br>Asn Ala<br>625  | agt gcc<br>Ser Ala          | Tyr Ser A                       | gca tat gcc<br>Ma Tyr Ala<br>330      | 1986   |
| tgc ttg gcc<br>Cys Leu Ala<br>635 | atc gtc a<br>lle Val                     | i e Phe P                     | tc tcc<br>he Ser<br>40     | gtt ctg<br>Val Leu          | ggc gtg g<br>Gly Val V<br>645   | tg ttt ggc<br>al Phe Gly              | 2034   |
| aaa ggg aac<br>Lys Gly Asn        | acg gcc t<br>Thr Ala F                   | tc tgg a<br>Phe Trp I         | tt gtc<br>ie Val i         | ttc tcc<br>Phe Ser          | gtc att c<br>Val lle H          | ac atc atc<br>is lle lle              | 2082   |



| tco<br>Ser<br>665 | ınr               | ctg<br>Leu        | cto<br>Leu        | cto<br>Lei        | ago<br>Ser<br>670 | lhr               | cag<br>Gln        | cto<br>Leu        | tat<br>Tyr        | tac<br>Tyr<br>675 | Met               | g ggc<br>E Gly    | cgc<br>Arg        | tgg<br>Trp        | g aag<br>Lys<br>680 | 2130 |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|---------------------|------|
| ctg<br>Leu        | gac<br>Asp        | ttc<br>Phe        | ggg<br>Gly        | ato<br>Ile<br>685 | Phe               | cgc<br>Arg        | cgc<br>Arg        | atc<br>Ile        | cto<br>Leu<br>690 | ı His             | gtg<br>Val        | g ctc<br>Leu      | tac<br>Tyr        | aca<br>Thr<br>695 | gac<br>Asp          | 2178 |
| tgc<br>Cys        | atc<br>lle        | cgg<br>Arg        | cag<br>Gln<br>700 | tgc<br>Cys        | agc<br>Ser        | ggg<br>Gly        | ccc<br>Pro        | ctt<br>Leu<br>705 | Tyr               | acg<br>Thr        | gac<br>Asp        | cgc<br>Arg        | atg<br>Met<br>710 | gtg<br>Val        | ctt<br>Leu          | 2226 |
| ctg<br>Leu        | gtc<br>Val        | atg<br>Met<br>715 | ggc<br>Gly        | aac<br>Asn        | att<br>lle        | atc<br>lle        | aac<br>Asn<br>720 | tgg<br>Trp        | tcg<br>Ser        | ctg<br>Leu        | gct<br>Ala        | gca<br>Ala<br>725 | tac<br>Tyr        | gga<br>Gly        | ctc<br>Leu          | 2274 |
| atc<br>lle        | atg<br>Met<br>730 | cgc<br>Arg        | ccc<br>Pro        | aat<br>Asn        | gac<br>Asp        | ttt<br>Phe<br>735 | gct<br>Ala        | tcc<br>Ser        | tac<br>Tyr        | ttg<br>Leu        | ctg<br>Leu<br>740 | gca<br>Ala        | att<br>Ile        | ggc<br>Gly        | atc<br>lle          | 2322 |
| tgc<br>Cys<br>745 | aac<br>Asn        | ctg<br>Leu        | ctg<br>Leu        | ctt<br>Leu        | tat<br>Tyr<br>750 | ttc<br>Phe        | gcc<br>Ala        | ttc<br>Phe        | tac<br>Tyr        | atc<br>Ile<br>755 | atc<br>Ile        | atg<br>Met        | aag<br>Lys        | ctc<br>Leu        | cgg<br>Arg<br>760   | 2370 |
| agc<br>Ser        | ggc<br>Gly        | gag<br>Glu        | agg<br>Arg        | atc<br>Ile<br>765 | aag<br>Lys        | ctc<br>Leu        | atc<br>lle        | cct<br>Pro        | ctg<br>Leu<br>770 | ctt<br>Leu        | tgc<br>Cys        | atc<br>lle        | gtc<br>Val        | tgc<br>Cys<br>775 | acc<br>Thr          | 2418 |
| tcc<br>Ser        | gtg<br>Val        | gtc<br>Val        | tgg<br>Trp<br>780 | ggc<br>Gly        | ttc<br>Phe        | gcg<br>Ala        | ctc<br>Leu        | ttc<br>Phe<br>785 | ttc<br>Phe        | ttc<br>Phe        | ttc<br>Phe        | cag<br>Gin        | gga<br>Gly<br>790 | ctg<br>Leu        | agc<br>Ser          | 2466 |
| acg<br>Thr        | irp               | cag<br>Gln<br>795 | aaa<br>Lys        | acc<br>Thr        | ccc<br>Pro        | gca<br>Ala        | gag<br>Glu<br>800 | tcc<br>Ser        | agg<br>Arg        | gag<br>Glu        | cac<br>His        | aac<br>Asn<br>805 | cgc<br>Arg        | gac<br>Asp        | tgc<br>Cys          | 2514 |
| Пe                | ctc<br>Leu<br>810 | ctc<br>Leu        | gac<br>Asp        | ttc<br>Phe        | Phe               | gat<br>Asp<br>815 | gac<br>Asp        | cac<br>His        | gat<br>Asp        | atc<br>He         | tgg<br>Trp<br>820 | cac<br>His        | ttc<br>Phe        | ctg<br>Leu        | tcc<br>Ser          | 2562 |
| tcc<br>Ser<br>825 | att<br>He         | gcc<br>Ala i      | atg<br>Met        | Phe               | ggg<br>Gly<br>830 | tcc<br>Ser        | ttc<br>Phe        | ctg<br>Leu        | Val               | ttg<br>Leu<br>835 | ctg<br>Leu        | acg<br>Thr        | ttg<br>Leu        | Asp               | gac<br>Asp<br>840   | 2610 |
| gac<br>Asp l      | ttg<br>Leu        | gac<br>Asp        | ihr \             | gta<br>Val<br>845 | cag<br>Gln ,      | cgg<br>Arg        | gac a<br>Asp l    | _ys               | atc<br>Ile<br>850 | tat<br>Tyr        | gtc<br>Val        | ttc<br>Phe        | tagc.             | agca              | tc                  | 2659 |
| tgtgg             | gtcca             | ag go             | cttca             | acct              | c ac              | gggc              | ctag              | cgc               | ctgc              | ctc               | tgca              | tcac              | ct go             | ccag              | ttgcc               | 2719 |
| acaag             | gaaca             | ac ca             | acggg             | gtgt              | g agt             | ccca              | agct              | ctgo              | ctgc              | сса               | gcat              | tgga              | tg to             | gtg               | gcaag               | 2779 |
| acago             | egaga             | at to             | cago              | cca               | g gcc             | etgad             | ctca              | ggad              | cagt <sup>.</sup> | tcc               | tggt              | ggcad             | ct ga             | agcc <sup>-</sup> | ttgga               | 2839 |
| gttgc             | ctct              | g cg              | gagg              | agga              | a ggo             | ctgo              | ctcc              | gcat              | ttcc              | cca ;             | gaca              | ctggo             | cc aa             | att               | gctgc               | 2899 |

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Glu Ser His Leu Gly Ala Leu Gly Pro Lys Asn Val Ser Gln Lys Asp 20 25 30

Ala Glu Phe Glu Arg Thr Tyr Ala Asp Asp Val Asn Ser Glu Leu Val 35 40 45

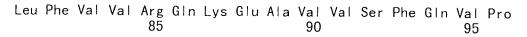
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Val Arg Val Ser Val Asn Val Leu Asn Lys Gln Lys Gly Ala Pro Leu

<sup>&</sup>lt;211> 853

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens



Leu lle Leu Arg Gly Leu Tyr Gln Arg Lys Tyr Leu Tyr Gln Lys Val 100 105 110

Glu Arg Thr Leu Cys Gln Pro Pro Thr Lys Asn Glu Ser Glu lle Gln 115 120 125

Phe Phe Tyr Val Asp Val Ser Thr Leu Ser Pro Val Asn Thr Tyr 130 135 140

Gln Leu Arg Val Asn Arg Val Asp Asn Phe Val Leu Arg Thr Gly Glu 145 150 155 160

Leu Phe Thr Phe Asn Thr Thr Ala Ala Gln Pro Gln Tyr Phe Lys Tyr 165 170 175

Glu Phe Pro Asp Gly Val Asp Ser Val IIe Val Lys Val Thr Ser Lys 180 185 190

Lys Ala Phe Pro Cys Ser Val IIe Ser IIe Gln Asp Val Leu Cys Pro 195 200 205

Val Tyr Asp Leu Asp Asn Ser Val Ala Phe Ile Gly Met Tyr Gln Thr 210 215 220

Met Thr Lys Lys Ala Ala lle Thr Val Gln Arg Lys Asp Phe Pro Ser 225 230 235 240

Asn Ser Phe Tyr Val Val Val Val Lys Thr Glu Asp Gln Ala Cys 245 250 255

Gly Gly Ser Leu Pro Phe Tyr Pro Phe Val Glu Asp Glu Pro Val Asp 260 265 270

Gln Gly His Arg Gln Lys Thr Leu Ser Val Leu Val Ser Gln Ala Val 275 280 285

Thr Ser Glu Ala Tyr Val Gly Gly Met Leu Phe Cys Leu Gly Ile Phe 290 295 300

Leu Ser Phe Tyr Leu Leu Thr Val Leu Leu Ala Cys Trp Glu Asn Trp 305 310 315 320

Arg Gln Arg Lys Lys Thr Leu Leu Val Ala lle Asp Arg Ala Cys Pro 325 330 335

Glu Ser Gly His Ala Arg Val Leu Ala Asp Ser Phe Pro Gly Ser Ala 340 345 350

Pro Tyr Glu Gly Tyr Asn Tyr Gly Ser Phe Glu Asn Gly Ser Gly Ser 355 360 365

Thr Asp Gly Leu Val Glu Ser Ala Gly Ser Gly Asp Leu Ser Tyr Ser 370 375 380

| Tyr<br>385 | Gln        | ∈G∃y       | His         | Asp        | GIn<br>390 | Phe        | Lys        | Arg        | Arg        | Leu<br>395 |            | Ser        | Gly        | Gln        | Met<br>400 |
|------------|------------|------------|-------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| Arg        | Gln        | Leu        | Cys         | 11e<br>405 | Ala        | Met        | Asp        | Arg        | Ser<br>410 |            | Asp        | Ala        | Val        | Gly<br>415 |            |
| Arg        | Pro        | Arg        | Leu<br>420  |            | Ser        | Met        | Ser        | Ser<br>425 |            | Glu        | Glu        | Asp        | Asp<br>430 | -          | Asp        |
| Thr        | Leu        | Thr<br>435 | Asp         | lle        | Asp        | Ser        | Asp<br>440 |            | Asn        | Val        | lle        | Arg<br>445 |            | Lys        | Gln        |
| Tyr        | Leu<br>450 | Cys        | Val         | Ala        | Asp        | Leu<br>455 | Ala        | Arg        | Lys        | Asp        | Lys<br>460 |            | Val        | Leu        | Arg        |
| Lys<br>465 | Lys        | Tyr        | Gln         | lle        | Tyr<br>470 | Phe        | Trp        | Asn        | lle        | Ala<br>475 |            | lle        | Ala        | Val        | Phe<br>480 |
| Tyr        | Ala        | Leu        | Pro         | Val<br>485 | Val        | Gln        | Leu        | Val        | 11e<br>490 | Thr        | Tyr        | Gln        | Thr        | Val<br>495 | Val        |
| Asn        | Val        | Thr        | Gly<br>500  | Asn        | Gln        | Asp        | Пе         | Cys<br>505 | Tyr        | Tyr        | Asn        | Phe        | Leu<br>510 | Cys        | Ala        |
| His        | Pro        | Leu<br>515 | Gly         | Asn        | Leu        | Ser        | Ala<br>520 | Phe        | Asn        | Asn        | He         | Leu<br>525 |            | Asn        | Leu        |
| Gly        | Tyr<br>530 | lle        | Leu         | Leu        | Gly        | Leu<br>535 | Leu        | Phe        | Leu        | Leu        | 11e<br>540 | lle        | Leu        | Gln        | Arg        |
| G1u<br>545 | He         | Asn        | His         | Asn        | Arg<br>550 | Ala        | Leu        | Leu        | Arg        | Asn<br>555 | Asp        | Leu        | Tyr        | Ala        | Leu<br>560 |
| Glu        | Cys        | Gly        | He          | Pro<br>565 | Lys        | His        | Phe        | Gly        | Leu<br>570 | Phe        | Tyr        | Ala        | Met        | Gly<br>575 | Thr        |
| Ala        | Leu        | Met        | Met<br>580  | Glu        | G∣y        | Leu        | Leu        | Ser<br>585 | Ala        | Cys        | Tyr        | His        | Val<br>590 | Cys        | Pro        |
| Asn        | Tyr        | Thr<br>595 | Asn         | Phe        | Gln        | Phe        | Asp<br>600 | Thr        | Ser        | Phe        | Met        | Tyr<br>605 | Met        | lle        | Ala        |
|            | Leu<br>610 | Cys        | Met         | Leu        | Lys        | Leu<br>615 | Tyr        | Gln        | Lys        | Arg        | His<br>620 | Pro        | Asp        | He         | Asn        |
| A∣a<br>625 | Ser        | Ala        | Tyr         | Ser        | Ala<br>630 | Tyr        | Ala        | Cys        | Leu        | Ala<br>635 | He         | Val        | He         | Phe        | Phe<br>640 |
| Ser        | Val        | Leu        | Gly         | Va!<br>645 | Val        | Phe        | Gly        | Lys        | Gly<br>650 | Asn        | Thr        | Ala        | Phe        | Trp<br>655 | lle        |
| √al        | Phe        | Ser        | Va l<br>660 | lle        | His        | Пe         |            | Ser<br>665 | Thr        | Leu        | Leu        | Leu        | Ser<br>670 | Thr        | Gln        |
| _eu        | Tyr        | Tyr<br>675 | Met         | Gly        | Arg        | Trp        | Lys<br>680 | Leu        | Asp        | Phe        | Gly        | lle<br>685 | Phe        | Arg        | Arg        |

| lle                          | Leu<br>690     | His            | Val                | Led              | _yr          | Thr<br>695 | Asp                       | Cys              | lle              | Arg          | GIn<br>700        | Cys            | \$               | Gly              | Pro                  |     |
|------------------------------|----------------|----------------|--------------------|------------------|--------------|------------|---------------------------|------------------|------------------|--------------|-------------------|----------------|------------------|------------------|----------------------|-----|
| Leu<br>705                   | Tyr            | Thr            | Asp                | Arg              | Met<br>710   | Val        | Leu                       | Leu              | Val              | Met<br>715   | Gly               | Asn            | lle              | He               | Asn<br>720           |     |
| Trp                          | Ser            | Leu            | Ala                | Ala<br>725       | Tyr          | Gly        | Leu                       | lle              | Met<br>730       | Arg          | Pro               | Asn            | Asp              | Phe<br>735       | Ala                  |     |
| Ser                          | Tyr            | Leu            | Leu<br>740         | Ala              | lle          | Gly        | lle                       | Cys<br>745       | Asn              | Leu          | Leu               | Leu            | Tyr<br>750       | Phe              | Ala                  |     |
| Phe                          | Tyr            | 11e<br>755     | He                 | Met              | Lys          | Leu        | Arg<br>760                | Ser              | Gly              | Glu          | Arg               | lle<br>765     | Lys              | Leu              | He                   |     |
| Pro                          | Leu<br>770     | Leu            | Cys                | lle              | Val          | Cys<br>775 | Thr                       | Ser              | Val              | Val          | Trp<br>780        | Gly            | Phe              | Ala              | Leu                  |     |
| Phe<br>785                   | Phe            | Phe            | Phe                | Gln              | Gly<br>790   | Leu        | Ser                       | Thr              | Trp              | Gin<br>795   | Lys               | Thr            | Pro              | Ala              | Glu<br>800           |     |
| Ser                          | Arg            | Glu            | His                | Asn<br>805       | Arg          | Asp        | Cys                       | lle              | Leu<br>810       | Leu          | Asp               | Phe            | Phe              | Asp<br>815       | Asp                  |     |
| His                          | Asp            | Пе             | Trp<br>820         | His              | Phe          | Leu        | Ser                       | Ser<br>825       | lle              | Ala          | Met               | Phe            | Gly<br>830       | Ser              | Phe                  |     |
| Leu                          | Val            | Leu<br>835     | Leu                | Thr              | Leu          | Asp        | Asp<br>840                | Asp              | Leu              | Asp          | Thr               | Val<br>845     | Gln              | Arg              | Asp                  |     |
|                              | lle<br>850     | Tyr            | Val                | Phe              |              |            |                           |                  |                  |              |                   |                |                  |                  |                      |     |
| <210<br><211<br><212<br><213 | > 31<br>> DN   | 38<br>A        | apie               | ns               |              |            |                           |                  |                  |              |                   |                |                  |                  |                      |     |
| <220;<br><221;<br><222;      | > CD           |                | (264               | 8)               |              |            |                           |                  |                  |              |                   |                |                  |                  |                      |     |
| <400)<br>gccg                |                |                | tccc               | ggag             | g tg         | tcct       | gtct                      | cct              | gtcg             | ccg          | ccgc              | cgcc           | gc c             | асса             | ccgct                | 60  |
| gcca                         | ctgc           | cg c           | cctg               | ccgg             | g gc         | c at<br>Me | g tt<br>t Ph<br>1         | c gc<br>e Al     | t ct<br>a Le     | g gg<br>u Gl | c tt<br>y Le<br>5 | g cc<br>u Pr   | c tt<br>o Ph     | c tt<br>e Le     | g gtg<br>u Val<br>10 | 113 |
| ctc t<br>_eu l               | ttg (<br>_eu \ | gtg ;<br>Val . | gcc<br>Ala         | tcg<br>Ser<br>15 | gtc .<br>Val | gag<br>Glu | agc<br>Ser                | cat<br>His       | ctg<br>Leu<br>20 | ggg<br>Gly   | gtt (<br>Val      | ctg<br>Leu     | ggg<br>Gly       | ccc<br>Pro<br>25 | aag<br>Lys           | 161 |
| aac g<br>Asn \               | gtc †<br>/al S | tog (<br>Ser ( | cag<br>Gln I<br>30 | aaa<br>Lys       | gac<br>Asp   | gcc<br>Ala | gag <sup>.</sup><br>Glu l | ttt<br>Phe<br>35 | gag<br>Glu       | cgc<br>Arg   | acc<br>Thr        | tac ;<br>Tyr ' | gtg<br>Val<br>40 | gac<br>Asp       | gag<br>Glu           | 209 |

|                   |            |            |            | •                 |                   |            |            |            |                   |                   |                   |            |            |                   |                   |     |
|-------------------|------------|------------|------------|-------------------|-------------------|------------|------------|------------|-------------------|-------------------|-------------------|------------|------------|-------------------|-------------------|-----|
|                   |            |            | Glu        |                   |                   |            |            | Tyr        |                   |                   | aac<br>Asn        |            | Thr        |                   |                   | 257 |
|                   |            | Arg        |            |                   |                   |            | Arg        |            |                   |                   | aac<br>Asn<br>70  |            |            |                   |                   | 305 |
|                   | Lys        |            |            |                   |                   | Leu        |            |            |                   |                   | cag<br>Gln        |            |            |                   |                   | 353 |
|                   |            |            |            |                   |                   |            |            |            |                   |                   | atg<br>Met        |            |            |                   |                   | 401 |
|                   |            |            |            |                   |                   |            |            |            |                   |                   | cag<br>Gln        |            |            |                   |                   | 449 |
|                   |            |            |            |                   |                   |            |            |            |                   |                   | gtg<br>Val        |            |            |                   |                   | 497 |
|                   |            | Asn        |            |                   |                   |            |            |            |                   |                   | cgc<br>Arg<br>150 |            |            |                   |                   | 545 |
|                   |            |            |            |                   |                   |            |            |            |                   |                   | acc<br>Thr        |            |            |                   |                   | 593 |
| ccc<br>Pro        | cag<br>Gin | tac<br>Tyr | ttc<br>Phe | aag<br>Lys<br>175 | tat<br>Tyr        | gag<br>G u | ttc<br>Phe | cct<br>Pro | gaa<br>Glu<br>180 | ggc<br>Gly        | gtg<br>Val        | gac<br>Asp | tcg<br>Ser | gta<br>Val<br>185 | att<br>He         | 641 |
|                   |            |            |            | Ser               | Asn               |            | Ala        |            |                   |                   | tca<br>Ser        |            |            |                   |                   | 689 |
|                   |            |            |            |                   |                   |            |            |            |                   |                   | aac<br>Asn        |            |            |                   |                   | 737 |
|                   |            |            |            |                   |                   |            |            |            |                   |                   | gcc<br>Ala<br>230 |            |            |                   |                   | 785 |
| cgc<br>Arg<br>235 | aaa<br>Lys | gac<br>Asp | ttc<br>Phe | ccc<br>Pro        | agc<br>Ser<br>240 | aac<br>Asn | agc<br>Ser | ttt<br>Phe | tat<br>Tyr        | gtg<br>Val<br>245 | gtg<br>Val        | gtg<br>Val | gtg<br>Val | gtg<br>Val        | aag<br>Lys<br>250 | 833 |
|                   |            |            | Gln        |                   |                   |            |            | Ser        |                   |                   | ttc<br>Phe        |            |            |                   |                   | 881 |
| gaa               | gat        | gaa        | ccg        | gtc               | gat               | caa        | ggg        | cac        | cgc               | cag               | aaa               | acc        | ctg        | tca               | gtg               | 929 |

|                   |                   |                        |                   |                   | _                 |                   |                     |                   |                   |                     | •                   |                    |                   |                       |                       |      |
|-------------------|-------------------|------------------------|-------------------|-------------------|-------------------|-------------------|---------------------|-------------------|-------------------|---------------------|---------------------|--------------------|-------------------|-----------------------|-----------------------|------|
| Glu               | ı Ası             | p Glu                  | 270<br>270        | o Va<br>0         |                   | o Glr             | n Gly               | / His<br>278      | s Arg             | g Glr               | n Ly                | s Th               | r<br>20           |                       | r Val                 |      |
| ctg<br>Leu        | g gtų<br>į Va     | g to<br>  Ser<br>  285 | 611               | a gca<br>n Ala    | a gto<br>a Val    | c acg             | g tot<br>Ser<br>290 | Glu               | g gca<br>ı Ala    | a tad<br>a Tyr      | c gte<br>Va         | c ag<br>I Se<br>29 | r Gl              | g at                  | g ctc<br>t Leu        | 977  |
| ttt<br>Phe        | tgo<br>Cys<br>300 | s Lei                  | g ggt<br>u Gly    | t ata<br>y lle    | a ttt<br>e Phe    | cto<br>Leu<br>305 | ı Ser               | ttt<br>Phe        | tac<br>Tyr        | ctg<br>Leu          | g ctg<br>Lei<br>310 | u Thi              | c gt<br>r Va      | c cte<br>  Lei        | c ctg<br>u Leu        | 1025 |
| gcc<br>Ala<br>315 | Cys               | tgg<br>Trp             | g gag<br>o Glu    | g aac<br>u Asr    | tgg<br>Trp<br>320 | ) Arg             | g cag<br>g Gln      | aag<br>Lys        | ; aag<br>Lys      | g aag<br>Lys<br>325 | Thi                 | c ctg<br>Lei       | g cti<br>ı Lei    | g gtø<br>u Va         | g gcc<br>I Ala<br>330 | 1073 |
| att<br>He         | gac<br>Asp        | cga<br>Arg             | gcc<br>Ala        | tgo<br>Cys<br>335 | Pro               | gaa<br>Glu        | agc<br>Ser          | ggt<br>Gly        | cac<br>His<br>340 | Pro                 | cga<br>Arg          | a gto<br>g Val     | ctg<br>Lei        | g got<br>u Ala<br>345 | t gat<br>a Asp        | 1121 |
| tct<br>Ser        | ttt<br>Phe        | cct<br>Pro             | ggo<br>Gly<br>350 | Ser               | tcc<br>Ser        | cct<br>Pro        | tat<br>Tyr          | gag<br>Glu<br>355 | ggt<br>Gly        | tac<br>Tyr          | aac<br>Asr          | tat<br>Tyr         | ggo<br>Gly<br>360 | / Ser                 | ttt<br>Phe            | 1169 |
| gag<br>Glu        | aat<br>Asn        | gtt<br>Val<br>365      | Ser               | gga<br>Gly        | tct<br>Ser        | acc<br>Thr        | gat<br>Asp<br>370   | ggt<br>Gly        | ctg<br>Leu        | gtt<br>Val          | gac<br>Asp          | ago<br>Ser<br>375  | Ala               | ggc<br>Gly            | act<br>Thr            | 1217 |
| ggg<br>Gly        | gac<br>Asp<br>380 | Leu                    | tct<br>Ser        | tac<br>Tyr        | ggt<br>Gly        | tac<br>Tyr<br>385 | cag<br>Gln          | ggg<br>Gly        | cac<br>His        | gac<br>Asp          | cag<br>Gln<br>390   | Phe                | aag<br>Lys        | cgg<br>Arg            | cgc<br>Arg            | 1265 |
| ctc<br>Leu<br>395 | ccc<br>Pro        | tct<br>Ser             | ggc<br>Gly        | cag<br>G n        | atg<br>Met<br>400 | cgg<br>Arg        | cag<br>Gln          | ctg<br>Leu        | tgc<br>Cys        | att<br>lle<br>405   | gcc<br>Ala          | atg<br>Met         | ggc<br>Gly        | cgc<br>Arg            | tcc<br>Ser<br>410     | 1313 |
| ttt<br>Phe        | gaa<br>Glu        | cct<br>Pro             | gta<br>Val        | ggt<br>Gly<br>415 | act<br>Thr        | cgg<br>Arg        | ccc<br>Pro          | cga<br>Arg        | gtg<br>Val<br>420 | gac<br>Asp          | tcc<br>Ser          | atg<br>Met         | agc<br>Ser        | tct<br>Ser<br>425     | gtg<br>Val            | 1361 |
| gag<br>Glu        | gag<br>Glu        | gat<br>Asp             | gac<br>Asp<br>430 | tac<br>Tyr        | gac<br>Asp        | aca<br>Thr        | Leu                 | acc<br>Thr<br>435 | gac<br>Asp        | atc<br>lle          | gat<br>Asp          | tcc<br>Ser         | gac<br>Asp<br>440 | aag<br>Lys            | aat<br>Asn            | 1409 |
| gtc<br>Val        | att<br>lle        | cgc<br>Arg<br>445      | acc<br>Thr        | aag<br>Lys        | caa<br>Gln        | lyr               | ctc<br>Leu<br>450   | tat<br>Tyr        | gtg<br>Val        | gct<br>Ala          | gac<br>Asp          | ctg<br>Leu<br>455  | gca<br>Ala        | cgg<br>Arg            | aag<br>Lys            | 1457 |
| Asp               | aag<br>Lys<br>460 | cgt<br>Arg             | gtt<br>Val        | ctg<br>Leu        | Arg               | aaa<br>Lys<br>465 | aag<br>Lys          | tac<br>Tyr        | cag<br>GIn        | Пe                  | tac<br>Tyr<br>470   | ttc<br>Phe         | tgg<br>Trp        | aac<br>Asn            | att<br>He             | 1505 |
| gcc<br>Ala<br>475 | acc<br>Thr        | att<br>He              | gct<br>Ala        | Val               | ttc<br>Phe<br>480 | tat<br>Tyr        | gcc<br>Ala          | ctt<br>Leu        | Pro               | gtg<br>Val<br>485   | gtg<br>Val          | cag<br>G n         | ctg<br>Leu        | gtg<br>Val            | atc<br>lle<br>490     | 1553 |
| acc<br>Thr        | tac<br>Tyr        | cag<br>Gln             | lhr               | gtg<br>Val<br>495 | gtg<br>Val        | aat<br>Asn        | gtc<br>Val          | Thr               | ggg<br>Gly<br>500 | aat<br>Asn          | cag<br>G n          | gac<br>Asp         | atc<br>lle        | tgc<br>Cys<br>505     | tac<br>Tyr            | 1601 |

|                   |                   |                   |                   | 1                 |                   |                   |                   |                   |                   |                   |                   |                   | 4                 |                   |                   |      |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| tac<br>Tyr        | aac<br>Asn        | ttc<br>Phe        | ctc<br>Leu<br>510 | Cys               | gcc<br>Ala        | cac<br>His        | cca<br>Pro        | ctg<br>Leu<br>515 | ggc<br>Gly        | aat<br>Asn        | ctc<br>Leu        | agc<br>Ser        | gcc<br>Ala<br>520 | Phe               | aac<br>Asn        | 1649 |
| aac<br>Asn        | atc<br>lle        | ctc<br>Leu<br>525 | agc<br>Ser        | aac<br>Asn        | ctg<br>Leu        | ggg<br>Gly        | tac<br>Tyr<br>530 | Пe                | ctg<br>Leu        | ctg<br>Leu        | ggg<br>Gly        | ctg<br>Leu<br>535 | ctt<br>Leu        | ttc<br>Phe        | ctg<br>Leu        | 1697 |
| ctc<br>Leu        | atc<br>Ile<br>540 | atc<br>Ile        | ctg<br>Leu        | caa<br>G n        | cgg<br>Arg        | gag<br>Glu<br>545 | atc<br>Ile        | aac<br>Asn        | cac<br>His        | aac<br>Asn        | cgg<br>Arg<br>550 | gcc<br>Ala        | ctg<br>Leu        | ctg<br>Leu        | cgc<br>Arg        | 1745 |
|                   | Asp               | ctc<br>Leu        |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | 1793 |
| ttc<br>Phe        | tac<br>Tyr        | gcc<br>Ala        | atg<br>Met        | ggc<br>Gly<br>575 | aca<br>Thr        | gcc<br>Ala        | ctg<br>Leu        | atg<br>Met        | atg<br>Met<br>580 | gag<br>Glu        | ggg<br>Gly        | ctg<br>Leu        | ctc<br>Leu        | agt<br>Ser<br>585 | gct<br>Ala        | 1841 |
| tgc<br>Cys        | tat<br>Tyr        | cat<br>His        | gtg<br>Val<br>590 | tgc<br>Cys        | ccc<br>Pro        | aac<br>Asn        | tat<br>Tyr        | acc<br>Thr<br>595 | aat<br>Asn        | ttc<br>Phe        | cag<br>Gln        | ttt<br>Phe        | gac<br>Asp<br>600 | aca<br>Thr        | tcg<br>Ser        | 1889 |
| ttc<br>Phe        | atg<br>Met        | tac<br>Tyr<br>605 | atg<br>Met        | atc<br>Ile        | gcc<br>Ala        | gga<br>Gly        | ctc<br>Leu<br>610 | tgc<br>Cys        | atg<br>Met        | ctg<br>Leu        | aag<br>Lys        | ctc<br>Leu<br>615 | tac<br>Tyr        | cag<br>Gln        | aag<br>Lys        | 1937 |
| cgg<br>Arg        | cac<br>His<br>620 | ccg<br>Pro        | gac<br>Asp        | atc<br>Ile        | aac<br>Asn        | gcc<br>Ala<br>625 | agc<br>Ser        | gcc<br>Ala        | tac<br>Tyr        | agt<br>Ser        | gcc<br>Ala<br>630 | tac<br>Tyr        | gcc<br>Ala        | tgc<br>Cys        | ctg<br>Leu        | 1985 |
| gcc<br>Ala<br>635 | att<br>He         | gtc<br>Val        | atc<br>lle        | ttc<br>Phe        | ttc<br>Phe<br>640 | tct<br>Ser        | gtg<br>Val        | ctg<br>Leu        | ggc<br>Gly        | gtg<br>Val<br>645 | gtc<br>Val        | ttt<br>Phe        | ggc<br>Gly        | aaa<br>Lys        | ggg<br>Gly<br>650 | 2033 |
| aac<br>Asn        | acg<br>Thr        | gcg<br>Ala        | ttc<br>Phe        | tgg<br>Trp<br>655 | atc<br>lle        | gtc<br>Val        | ttc<br>Phe        | tcc<br>Ser        | atc<br>lle<br>660 | att<br>Ile        | cac<br>His        | atc<br>lle        | atc<br>He         | gcc<br>Ala<br>665 | acc<br>Thr        | 2081 |
| ctg<br>Leu        | ctc<br>Leu        | ctc<br>Leu        | agc<br>Ser<br>670 | acg<br>Thr        | cag<br>Gln        | ctc<br>Leu        | tat<br>Tyr        | tac<br>Tyr<br>675 | atg<br>Met        | ggc<br>Gly        | cgg<br>Arg        | tgg<br>Trp        | aaa<br>Lys<br>680 | ctg<br>Leu        | gac<br>Asp        | 2129 |
| tcg<br>Ser        | ggg<br>Gly        | atc<br>Ile<br>685 | ttc<br>Phe        | cgc<br>Arg        | cgc<br>Arg        | atc<br>lle        | ctc<br>Leu<br>690 | cac<br>His        | gtg<br>Val        | ctc<br>Leu        | tac<br>Tyr        | aca<br>Thr<br>695 | gac<br>Asp        | tgc<br>Cys        | atc<br>lle        | 2177 |
| Arg               | cag<br>Gln<br>700 | tgc<br>Cys        | agc<br>Ser        | ggg<br>Gly        | ccg<br>Pro        | ctc<br>Leu<br>705 | tac<br>Tyr        | gtg<br>Va!        | gac<br>Asp        | cgc<br>Arg        | atg<br>Met<br>710 | gtg<br>Val        | ctg<br>Leu        | ctg<br>Leu        | gtc<br>Val        | 2225 |
| atg<br>Met<br>715 | ggc<br>Gly        | aac<br>Asn        | gtc<br>Val        | atc<br>lle        | aac<br>Asn<br>720 | tgg<br>Trp        | tcg<br>Ser        | ctg<br>Leu        | gct<br>Ala        | gcc<br>Ala<br>725 | tat<br>Tyr        | ggg<br>Gly        | ctt<br>Leu        | atc<br>lle        | atg<br>Met<br>730 | 2273 |
| cgc               | ссс               | aat               | gat               | ttc               | gct               | tcc               | tac               | ttg               | ttg               | gcc               | att               | ggc               | atc               | tgc               | aac               | 2321 |

| Arg Pro Asn   | Asn Phe                   | Ser                       | Tyr Le                  | ينم ايند               | οιΔ               | ,<br>Ha           | GLV               |                   | .v.c        | Aon               |      |
|---|---------------------------|---------------------------|-------------------------|------------------------|-------------------|-------------------|-------------------|-------------------|-------------|-------------------|------|
| Alg 110 Asil  | 735                       | a der                     | Tyr L                   | 740                    | Ма                | 116               | ату               |                   | 745         | Asn               |      |
| ctg ctc ctt<br>Leu Leu Leu                          | tac ttc<br>Tyr Phe<br>750 | gcc ttc<br>Ala Phe        | Tyr I                   | tc atc<br>le lle<br>55 | atg<br>Met        | aag<br>Lys        | ctc<br>Leu        | cgg<br>Arg<br>760 | agt<br>Ser  | ggg<br>Gly        | 2369 |
| gag agg atc<br>Glu Arg lle<br>765                   | aag ctc<br>Lys Leu        | atc ccc<br>lle Pro        | ctg ct<br>Leu Le<br>770 | tc tgc<br>eu Cys       | atc<br>lle        | gtt<br>Val        | tgc<br>Cys<br>775 | acc<br>Thr        | tcc<br>Ser  | gtg<br>Val        | 2417 |
| gtc tgg ggc<br>Val Trp Gly<br>780                   | ttc gcg<br>Phe Ala        | ctc ttc<br>Leu Phe<br>785 | ttc tt<br>Phe Ph        | tc ttc<br>ne Phe       | cag<br>Gln        | gga<br>Gly<br>790 | ctc<br>Leu        | agc<br>Ser        | acc<br>Thr  | tgg<br>Trp        | 2465 |
| cag aaa acc<br>Gln Lys Thr<br>795                   | cct gca<br>Pro Ala        | gag tcg<br>Glu Ser<br>800 | agg ga<br>Arg G         | ag cac<br>Iu His       | aac<br>Asn<br>805 | cgg<br>Arg        | gac<br>Asp        | tgc<br>Cys        | atc<br>Ile  | ctc<br>Leu<br>810 | 2513 |
| ctc gac ttc<br>Leu Asp Phe                          |                           |                           |                         |                        |                   |                   |                   |                   |             |                   | 2561 |
| gcc atg ttc<br>Ala Met Phe                          |                           |                           |                         | er Gly                 |                   |                   |                   |                   |             |                   | 2609 |
| tgg gta cgt<br>Trp Val Arg<br>845                   |                           |                           |                         |                        |                   | Cys               |                   | tgat              | ctgg        | cg                | 2658 |
| tccacacccc a  | nggtgttgd                 | ct gacact                 | ggat g                  | acgaco                 | tgg               | atac              | ttag              | aa a              | gggg        | cttca             | 2718 |
| ggaagggatg t  | gctgtttc                  | c ctctac                  | gtgc c                  | cagtco                 | tag               | cctc              | gctc              | ta g              | gacc        | caggg             | 2778 |
| ctggcttcta a  | gtttccgt                  | c cagtct                  | tcag g                  | caagtt                 | ctg               | tgtt              | agtc              | at g              | caca        | cacat             | 2838 |
| acctatgaaa c  | cttggagt                  | t tacaaa                  | agaat t                 | gcccca                 | gct               | ctgg              | gcac              | cc t              | ggcc        | accct             | 2898 |
| ggtccttgga t  | ccccttcg                  | t cccacc                  | tggt c                  | cacccc                 | aga               | tgct              | gagg              | at g              | gggg        | agctc             | 2958 |
| aggcggggcc t  | ctgctttg                  | g ggatgg                  | gaat g                  | tgtttt                 | tct               | ссса              | aact              | tg t              | tttt        | atagc             | 3018 |
| tctgcttgaa g  | ggctggga                  | ig atgagg                 | tggg t                  | ctggat                 | ctt               | ttct              | caga              | gc g              | tctc        | catgc             | 3078 |
| tatggttgca t  | ttccgttt                  | t ctatga                  | atga a                  | tttgca                 | ttc               | aata              | aaca              | ас с              | agac        | tcagt             | 3138 |
| <210> 166<br><211> 855<br><212> PRT<br><213> Homo s | apiens                    |                           |                         |                        |                   |                   |                   |                   |             |                   |      |
| <400> 166<br>Met Phe Ala<br>1                       | Leu Gly<br>5              | Leu Pro                   | Phe Le                  | u Val<br>10            | Leu               | Leu               | Val               | Ala               | Ser '<br>15 | Val               |      |

Glu Ser His Leu Gly Val Leu Gly Pro Lys Asn Val Ser Gln Lys Asp

- Ala Glu Phe Glu Arg Thr Tyr Val Asp Glu Val Asn Ser Glu Leu Val Asn lle Tyr Thr Phe Asn His Thr Val Thr Arg Asn Arg Thr Glu Gly Val Arg Val Ser Val Asn Val Leu Asn Lys Gln Lys Gly Ala Pro Leu Leu Phe Val Val Arg Gin Lys Glu Ala Val Val Ser Phe Gin Val Pro Leu lle Leu Arg Gly Met Phe Gln Arg Lys Tyr Leu Tyr Gln Lys Val Glu Arg Thr Leu Cys Gln Pro Pro Thr Lys Asn Glu Ser Glu lle Gln Phe Phe Tyr Val Asp Val Ser Thr Leu Ser Pro Val Asn Thr Thr Tyr 135 Gin Leu Arg Val Ser Arg Met Asp Asp Phe Val Leu Arg Thr Gly Glu Gin Phe Ser Phe Asn Thr Thr Ala Ala Gin Pro Gin Tyr Phe Lys Tyr 170 Glu Phe Pro Glu Gly Val Asp Ser Val IIe Val Lys Val Thr Ser Asn 180 Lys Ala Phe Pro Cys Ser Val Ile Ser Ile Gln Asp Val Leu Cys Pro 200 Val Tyr Asp Leu Asp Asn Asn Val Ala Phe lle Gly Met Tyr Gln Thr 210 Met Thr Lys Lys Ala Ala Ile Thr Val Gln Arg Lys Asp Phe Pro Ser Asn Ser Phe Tyr Val Val Val Val Lys Thr Glu Asp Gln Ala Cys Gly Gly Ser Leu Pro Phe Tyr Pro Phe Ala Glu Asp Glu Pro Val Asp Gln Gly His Arg Gln Lys Thr Leu Ser Val Leu Val Ser Gln Ala Val 280 Thr Ser Glu Ala Tyr Val Ser Gly Met Leu Phe Cys Leu Gly lle Phe 290 295 300 Leu Ser Phe Tyr Leu Leu Thr Val Leu Leu Ala Cys Trp Glu Asn Trp
- Arg Gln Lys Lys Thr Leu Leu Val Ala He Asp Arg Ala Cys Pro 325 330 335

Glu Ser Gly His Pro Arg Val Leu Ala Asp Ser Phe Pro Gly Ser Ser 345 Pro Tyr Glu Gly Tyr Asn Tyr Gly Ser Phe Glu Asn Val Ser Gly Ser 360 Thr Asp Gly Leu Val Asp Ser Ala Gly Thr Gly Asp Leu Ser Tyr Gly Tyr Gln Gly His Asp Gln Phe Lys Arg Arg Leu Pro Ser Gly Gln Met Arg Gin Leu Cys lie Ala Met Gly Arg Ser Phe Glu Pro Val Gly Thr Arg Pro Arg Val Asp Ser Met Ser Ser Val Glu Glu Asp Asp Tyr Asp 425 Thr Leu Thr Asp Ile Asp Ser Asp Lys Asn Val Ile Arg Thr Lys Gln Tyr Leu Tyr Val Ala Asp Leu Ala Arg Lys Asp Lys Arg Val Leu Arg Lys Lys Tyr Gin ile Tyr Phe Trp Asn ile Ala Thr ile Ala Val Phe 465 Tyr Ala Leu Pro Val Val Gln Leu Val Ile Thr Tyr Gln Thr Val Val Asn Val Thr Gly Asn Gln Asp lle Cys Tyr Tyr Asn Phe Leu Cys Ala His Pro Leu Gly Asn Leu Ser Ala Phe Asn Asn Ile Leu Ser Asn Leu 520 Gly Tyr lle Leu Leu Gly Leu Leu Phe Leu Leu IIe lle Leu Gln Arg 530 535 540 Glu lle Asn His Asn Arg Ala Leu Leu Arg Asn Asp Leu Cys Ala Leu Glu Cys Gly lle Pro Lys His Phe Gly Leu Phe Tyr Ala Met Gly Thr Ala Leu Met Met Glu Gly Leu Leu Ser Ala Cys Tyr His Val Cys Pro 580 Asn Tyr Thr Asn Phe Gln Phe Asp Thr Ser Phe Met Tyr Met Ile Ala 600 Gly Leu Cys Met Leu Lys Leu Tyr Gln Lys Arg His Pro Asp lle Asn 610 615 620 Ala Ser Ala Tyr Ser Ala Tyr Ala Cys Leu Ala IIe Val IIe Phe Phe 625

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Ser Val Leu Gly Va Pal Phe Gly Lys Gly Asn Thr Ala
                                                         655
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Val Phe Ser Ile Ile His Ile Ile Ala Thr Leu Leu Leu Ser Thr Gln
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Leu Tyr Tyr Met Gly Arg Trp Lys Leu Asp Ser Gly Ile Phe Arg Arg
lle Leu His Val Leu Tyr Thr Asp Cys lle Arg Gln Cys Ser Gly Pro
                        695
Leu Tyr Val Asp Arg Met Val Leu Leu Val Met Gly Asn Val Ile Asn
Trp Ser Leu Ala Ala Tyr Gly Leu lle Met Arg Pro Asn Asp Phe Ala
                                    730
Ser Tyr Leu Leu Ala Ile Gly Ile Cys Asn Leu Leu Leu Tyr Phe Ala
Phe Tyr lle lle Met Lys Leu Arg Ser Gly Glu Arg lle Lys Leu lle
Pro Leu Leu Cys Ile Vai Cys Thr Ser Val Val Trp Gly Phe Ala Leu
Phe Phe Phe Gln Gly Leu Ser Thr Trp Gln Lys Thr Pro Ala Glu
                                        795
                    790
Ser Arg Glu His Asn Arg Asp Cys IIe Leu Leu Asp Phe Phe Asp Asp
                                    810
His Asp lle Trp His Phe Leu Ser Ser lle Ala Met Phe Gly Ser Phe
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| gag tgc aca gaa gcc aaa aag cat tgc tgg tat ttc gaa gga ctc tat 154<br>Glu Cys Thr Glu Ala Lys Lys His Cys Trp Tyr Phe Glu Gly Leu Tyr<br>20 25 30    |  |
| cca acc tat tat ata tgc cgc tcc tac gag gac tgc tgt ggc tcc agg 202 Pro Thr Tyr Tyr lle Cys Arg Ser Tyr Glu Asp Cys Cys Gly Ser Arg 35 40 45          |  |
| tgc tgt gtg cgg gcc ctc tcc ata cag agg ctg tgg tac ttc tgg ttc  Cys Cys Val Arg Ala Leu Ser lle Gln Arg Leu Trp Tyr Phe Trp Phe  50 65               |  |
| ctt ctg atg atg ggc gtg ctt ttc tgc tgc gga gcc ggc ttc ttc atc 298<br>Leu Leu Met Met Gly Val Leu Phe Cys Cys Gly Ala Gly Phe Phe Ile<br>70 75 80    |  |
| cgg agg cgc atg tac ccc ccg ccg ctg atc gag gag cca gcc ttc aat Arg Arg Arg Met Tyr Pro Pro Pro Leu IIe Glu Glu Pro Ala Phe Asn 85 90 95              |  |
| gtg tcc tac acc agg cag ccc cca aat ccc ggc cca gga gcc cag cag 394<br>Val Ser Tyr Thr Arg Gln Pro Pro Asn Pro Gly Pro Gly Ala Gln Gln<br>100 105 110 |  |
| ccg ggg ccg ccc tat tac acc gac cca gga gga ccg ggg atg aac cct Pro Gly Pro Pro Tyr Tyr Thr Asp Pro Gly Gly Pro Gly Met Asn Pro 115 120 125           |  |
| gtc ggg aat tcc atg gca atg gct ttc cag gtc cca ccc aac tca ccc Val Gly Asn Ser Met Ala Met Ala Phe Gln Val Pro Pro Asn Ser Pro 130 145               |  |
| cag ggg agt gtg gcc tgc ccg ccc cct cca gcc tac tgc aac acg cct 538<br>Gln Gly Ser Val Ala Cys Pro Pro Pro Pro Ala Tyr Cys Asn Thr Pro<br>150 155 160 |  |
| ccg ccc ccg tac gaa cag gta gtg aag gcc aag tagtggggtg cccacgtgca 591<br>Pro Pro Pro Tyr Glu Gin Val Val Lys Ala Lys<br>165 170                       |  |
| agaggaggga caggagaggg cctttccctg gcctttctgt cttcgttgat gttcacttcc 651   |  |
| aggaacggtc tcgtgggctg ctaagggcag ttcctctgat atcctcacag caagcacagc 711   |  |
| tctctttcag gctttccatg gagtacaata tatgaactca cactttgtct cctctgttgc 771   |  |
| ttctgtttct gacgcagtct gtgctctcac atggtagtgt ggtgacagtc cccgagggct 831   |  |
| gacgtcctta cggtggcgtg accagatcta cgggagagag actgagagga agaaggcagt 891   |  |
| gctggaggtg caggtggcat gtagaggggc caggccgagc atcccaggca agcatccttc 951   |  |
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gggc

2815

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Tyr Pro Thr Tyr Tyr lle Cys Arg Ser Tyr Glu Asp Cys Cys Gly Ser 35 40 45

Arg Cys Cys Val Arg Ala Leu Ser lle Gln Arg Leu Trp Tyr Phe Trp 50 55 60

Phe Leu Leu Met Met Gly Val Leu Phe Cys Cys Gly Ala Gly Phe Phe 65 70 75 80

lle Arg Arg Met Tyr Pro Pro Pro Leu lle Glu Glu Pro Ala Phe 85 90 95

Asn Val Ser Tyr Thr Arg Gln Pro Pro Asn Pro Gly Pro Gly Ala Gln 100 105 110

Gln Pro Gly Pro Pro Tyr Tyr Thr Asp Pro Gly Gly Pro Gly Met Asn 115 120 125

Pro Val Gly Asn Ser Met Ala Met Ala Phe Gln Val Pro Pro Asn Ser 130 135 140

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|------------|-------------------|------------|------------|------------|-------------------|-------------------|------------|------------|------------|------------|-------------------|------------|------------|------------|----------------|-----|
| aga        | atct              | gag        | cagc       |            |                   |                   |            |            |            |            |                   |            |            | s Ty       | t atc<br>r lle | 171 |
|            |                   |            | Phe        |            | aat<br>Asn        |                   |            | Asn        |            |            |                   |            |            |            | ctg<br>Leu     | 219 |
|            |                   | Leu        |            |            | ctc<br>Leu        |                   |            |            |            |            |                   |            |            |            |                | 267 |
|            | Cys               |            |            |            | ggg<br>Gly<br>50  |                   |            |            |            |            |                   |            |            |            |                | 315 |
|            |                   |            |            |            | ccc<br>Pro        |                   |            |            |            |            |                   |            |            |            |                | 363 |
|            |                   |            |            |            | gtt<br>Val        |                   |            |            |            |            |                   |            |            |            |                | 411 |
|            |                   |            |            |            | cgg<br>Arg        |                   |            |            |            |            |                   |            |            |            |                | 459 |
|            |                   |            |            |            | gct<br>Ala        |                   |            |            |            |            |                   |            |            |            |                | 507 |
|            |                   |            |            |            | tac<br>Tyr<br>130 |                   |            |            |            |            |                   |            |            |            |                | 555 |
|            |                   |            |            |            | gag<br>Glu        |                   |            |            |            |            |                   |            |            |            |                | 603 |
|            |                   |            |            |            | cag<br>G n        |                   |            |            |            |            |                   |            |            |            |                | 651 |
|            |                   |            |            |            | ctg<br>Leu        |                   |            |            |            |            |                   |            |            |            |                | 699 |
| cct<br>Pro | ctg<br>Leu<br>190 | acc<br>Thr | tcc<br>Ser | agc<br>Ser | ggg<br>Gly        | cat<br>His<br>195 | cag<br>Gln | gag<br>Glu | cag<br>Gln | gac<br>Asp | aca<br>Thr<br>200 | gaa<br>Glu | ctg<br>Leu | ggc<br>Gly | 0              | 747 |
|            |                   |            |            |            | gcg<br>Ala<br>210 |                   |            |            |            |            |                   |            |            |            |                | 795 |

|            |            |                   |            | gtc<br>Val<br>225 | Ser        | ttc<br>Phe | cag<br>Gln        | ccc<br>Pro | ctg<br>Leu<br>230 | gcc<br>Ala | cgt<br>Arg | tcc<br>Ser        | a.<br>Thr  | Pro<br>235        | agg<br>Arg | 843  |
|------------|------------|-------------------|------------|-------------------|------------|------------|-------------------|------------|-------------------|------------|------------|-------------------|------------|-------------------|------------|------|
|            |            |                   |            | cct<br>Pro        |            |            |                   |            |                   |            |            |                   |            |                   |            | 891  |
| tcc<br>Ser | ttc<br>Phe | tcc<br>Ser<br>255 | tcc<br>Ser | tca<br>Ser        | tcc<br>Ser | cct<br>Pro | ggc<br>Gly<br>260 | ttg<br>Leu | gcc<br>Ala        | tct<br>Ser | gca<br>Ala | ggg<br>G y<br>265 | gct<br>Ala | gca<br>Ala        | gag<br>Glu | 939  |
|            |            |                   |            | gca<br>Ala        |            |            |                   |            |                   |            |            |                   |            |                   |            | 987  |
|            |            |                   |            | gca<br>Ala        |            |            |                   |            |                   |            |            |                   |            |                   |            | 1035 |
| acc<br>Thr | ttg<br>Leu | atg<br>Met        | cct<br>Pro | gtg<br>Val<br>305 | aac<br>Asn | aca<br>Thr | gtg<br>Va         | gcc<br>Ala | ctg<br>Leu<br>310 | aaa<br>Lys | gtg<br>Val | cct<br>Pro        | gcc<br>Ala | aac<br>Asn<br>315 | cca<br>Pro | 1083 |
|            |            |                   |            | aca<br>Thr        |            |            |                   |            |                   |            |            |                   |            |                   |            | 1131 |
|            |            |                   |            | cct<br>Pro        |            |            |                   |            |                   |            |            |                   |            |                   |            | 1179 |
|            |            |                   |            | tca<br>Ser        |            |            |                   |            |                   |            |            |                   |            |                   |            | 1227 |
|            | Ser        |                   | Val        | ctc<br>Leu        | Thr        | Lys        | Val               | Ser        | Ala               |            | Thr        |                   |            |                   |            | 1275 |
|            |            |                   |            | aat<br>Asn<br>385 |            |            |                   |            |                   |            |            |                   |            |                   |            | 1323 |
|            |            |                   |            | agc<br>Ser        |            |            |                   |            |                   |            |            |                   |            |                   |            | 1371 |
|            |            |                   |            | gag<br>Glu        |            |            |                   |            |                   |            |            |                   |            |                   |            | 1419 |
|            |            |                   |            | tcg<br>Ser        |            |            |                   |            |                   |            |            |                   |            |                   |            | 1467 |
|            |            |                   |            | atg<br>Met        |            |            |                   |            |                   |            |            |                   |            |                   |            | 1515 |

| 440                               |                                 | -0                              |                           | 100                     |                               |                           |      |
|-----------------------------------|---------------------------------|---------------------------------|---------------------------|-------------------------|-------------------------------|---------------------------|------|
| aag too gag<br>Lys Ser Glu        | ggc acc tt<br>Gly Thr Ph<br>465 | t ggg atc<br>ne Gly lle         | cac gtg<br>His Val<br>470 | gct gag<br>Ala Gli      | g aac ccc<br>u Asn Pro        | 0 -                       | 1563 |
| cag ctc ctg<br>Gln Leu Leu        | gag ggc aa<br>Glu Gly As<br>480 | ac cct ggg<br>an Pro Gly        | cca cct<br>Pro Pro<br>485 | gcg gad<br>Ala Asp      | c ccg gat<br>p Pro Asp<br>490 | Gly Gly                   | 1611 |
| ccc agg cca<br>Pro Arg Pro<br>495 | Gln Ala A                       | ac cgg aag<br>sp Arg Lys<br>500 | Phe Gln                   | gag ag<br>Glu Ar        | g gag gtg<br>g Glu Val<br>505 | cca tgc<br>Pro Cys        | 1659 |
| cac agg ccc<br>His Arg Pro<br>510 | tca cct g<br>Ser Pro G          | gg gct ctg<br>ly Ala Leu<br>515 | tgg ctc<br>Trp Leu        | cag gt<br>Gln Va<br>52  | l Ala Val                     | aca ggg<br>Thr Gly        | 1707 |
| gtg ctg gta<br>Val Leu Val<br>525 | Val Thr L                       | tc ctg gtg<br>eu Leu Val<br>30  | gtg ctg<br>Val Leu        | tac cg<br>Tyr Ar<br>535 | g cgg cgt<br>g Arg Arg        | ctg cac<br>Leu His<br>540 | 1755 |
| tagtgaagcc                        | ctgggctctt                      | cccaccacc                       | c atctgt                  | tccg tt                 | cctgcagt                      | atacctggcc                | 1815 |
| cctctccgaa                        | gcccctcttt                      | ccctcccct                       | c tggtct                  | ccat tc                 | tcttcagc                      | tccctacatg                | 1875 |
| ggctggggag                        | gagacacctg                      | gtgggcaga                       | g ctcagg                  | caga gg                 | tttggatt                      | tcagctccct                | 1935 |
| cacttccggg                        | gctgtgtggc                      | tttggcaga                       | t gtcaga                  | cttc tg                 | gtcttgct                      | tctccacgtg                | 1995 |
| gacagtgagt                        | atctggctca                      | ttcttcact                       | g ggttct                  | tctg ag                 | attgaacc                      | tacaggtgtt                | 2055 |
| tgccaagtgc                        | ctggcccaga                      | gcaagtggc                       | c actgct                  | tctc cc                 | atctctct                      | cctgcccaac                | 2115 |
| ctggtagagc                        | tgagggcatg                      | agaggcaga                       | ıg tgcaca                 | gtgg tc                 | aagggtgc                      | agctctgcgg                | 2175 |
| cacaggcagc                        | ctaggcctgc                      | gtcccaaco                       | t gcctct                  | cacc ag                 | ctctgtga                      | ccttgggcaa                | 2235 |
| gggatttatc                        | tgtctgtccc                      | ttagttttc                       | t cacctg                  | taaa ag                 | gaggataa                      | gtatatatat                | 2295 |
| atatttccca                        | gtgttgtgaa                      | gattaaagg                       | ga gtttat                 | cgat gt                 | aggtctta                      | ggatgagtcc                | 2355 |
| tggcatttac                        | caagggttgg                      | atatatgtt                       | a ttatca                  | ctat ta                 | agtgttga                      | gggtccaggc                | 2415 |
| atgctgggca                        | acagggaccc                      | catctctac                       | ca aaaaag                 | ttta aa                 | aaattagc                      | caggcgtggt                | 2475 |
| ggtgcacctg                        | togtottago                      | tacttggga                       | ag gctgag                 | gtgg ga                 | aggatcgct                     | tgagcccgga                | 2535 |
|                                   |                                 |                                 |                           |                         |                               | tgagagagcg                |      |
|                                   |                                 |                                 |                           |                         |                               | actcctttag                |      |
|                                   |                                 |                                 |                           |                         |                               | ttactttatc                |      |
|                                   |                                 |                                 |                           |                         |                               | tacaggatgg                |      |
|                                   |                                 |                                 |                           |                         |                               | tcacccactg                |      |
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Cys Leu Thr Ala Arg Asp Gln Asp Arg Leu Arg Ala Thr Cys Thr Leu 35 40 45

Ser Gly Asn Arg Asp Thr Leu Trp His Leu Phe Asn Thr Leu Gln Arg 50 55 60

Arg Pro Gly Trp Val Glu Tyr Phe lle Ala Ala Leu Arg Gly Cys Glu 65 70 75 80

Leu Val Asp Leu Ala Asp Glu Val Ala Ser Val Tyr Gln Ser Tyr Gln 85 90 95

Pro Arg Thr Ser Asp Arg Pro Pro Asp Pro Leu Glu Pro Pro Ser Leu 100 105 110

Pro Ala Glu Arg Pro Gly Pro Pro Thr Pro Ala Ala His Ser Ile 115 120 125

Pro Tyr Asn Ser Cys Arg Glu Lys Glu Pro Ser Tyr Pro Met Pro Val 130 135 140

Gln Glu Thr Gln Ala Pro Glu Ser Pro Gly Glu Asn Ser Glu Gln Ala 145 150 155 160

Leu Gln Thr Leu Ser Pro Arg Ala Ile Pro Arg Asn Pro Asp Gly Gly 165 170 175

| Pro         | Leu        | Glu        | Ser<br>180 | Se         | er          | Asp        | Leu        | Ala<br>185 | Ala        | Leu        | Ser        | Pro        | 190        | Thr        | Ser        |
|-------------|------------|------------|------------|------------|-------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| Ser         | Gly        | His<br>195 | Gln        | Glu        | Gln         | Asp        | Thr<br>200 | Glu        | Leu        | Gly        | Ser        | Thr<br>205 | His        | Thr        | Ala        |
| Gly         | Ala<br>210 | Thr        | Ser        | Ser        | Leu         | Thr<br>215 | Pro        | Ser        | Arg        | Gly        | Pro<br>220 | Val        | Ser        | Pro        | Ser        |
| Va I<br>225 | Ser        | Phe        | Gln        | Pro        | Leu<br>230  | Ala        | Arg        | Ser        | Thr        | Pro<br>235 | Arg        | Ala        | Ser        | Arg        | Leu<br>240 |
| Pro         | Gly        | Pro        | Thr        | Gly<br>245 | Ser         | Val        | Val        | Ser        | Thr<br>250 | Gly        | Thr        | Ser        | Phe        | Ser<br>255 | Ser        |
| Ser         | Ser        | Pro        | Gly<br>260 | Leu        | Ala         | Ser        | Ala        | Gly<br>265 | Ala        | Ala        | Glu        | Gly        | Lys<br>270 | Gln        | Gly        |
| Ala         | Glu        | Ser<br>275 | Asp        | Gln        | Ala         | Glu        | Pro<br>280 | lle        | lle        | Cys        | Ser        | Ser<br>285 | Gly        | Ala        | Glu        |
| Ala         | Pro<br>290 | Ala        | Asn        | Ser        | Leu         | Pro<br>295 | Ser        | Lys        | Val        | Pro        | Thr<br>300 | Thr        | Leu        | Met        | Pro        |
| Val<br>305  | Asn        | Thr        | Val        | Ala        | Leu<br>310  | Lys        | Val        | Pro        | Ala        | Asn<br>315 | Pro        | Ala        | Ser        | Val        | Ser<br>320 |
| Thr         | Val        | Pro        | Ser        | Lys<br>325 | Leu         | Pro        | Thr        | Ser        | Ser<br>330 | Lys        | Pro        | Pro        | Gly        | Ala<br>335 | Val        |
| Pro         | Ser        | Asn        | Ala<br>340 | Leu        | Thr         | Asn        | Pro        | Ala<br>345 | Pro        | Ser        | Lys        | Leu        | Pro<br>350 | He         | Asn        |
| Ser         | Thr        | Arg<br>355 | Ala        | Gly        | Met         | Val        | Pro<br>360 | Ser        | Lys        | Val        | Pro        | Thr<br>365 | Ser        | Met        | Val        |
| Leu         | Thr<br>370 | Lys        | Val        | Ser        | Ala         | Ser<br>375 | Thr        | Val        | Pro        | Thr        | Asp<br>380 | Gly        | Ser        | Ser        | Arg        |
| Asn<br>385  | Glu        | Glu        | Thr        | Pro        | Ala<br>390  | Ala        | Pro        | Thr        | Pro        | Ala<br>395 | Gly        | Ala        | Thr        | Gly        | Gly<br>400 |
| Ser         | Ser        | Ala        | Trp        | Leu<br>405 | Asp         | Ser        | Ser        | Ser        | Glu<br>410 | Asn        | Arg        | Gly        | Leu        | Gly<br>415 | Ser        |
| G∣u         | Leu        | Ser        | Lys<br>420 | Pro        | Gly         | Val        | Leu        | Ala<br>425 | Ser        | Gln        | Val        | Asp        | Ser<br>430 | Pro        | Phe        |
| Ser         | Gly        | Cys<br>435 | Phe        | Glu        | Asp         | Leu        | Ala<br>440 | He         | Ser        | Ala        | Ser        | Thr<br>445 | Ser        | Leu        | Gly        |
| Met         | Gly<br>450 | Pro        | Cys        | His        | Gly         | Pro<br>455 | Glu        | Glu        | Asn        | Glu        | Tyr<br>460 | Lys        | Ser        | Glu        | Gly        |
| Thr<br>465  | Phe        | Gly        | He         | His        | Va l<br>470 | Ala        | Glu        | Asn        | Pro        | Ser<br>475 | lle        | Gln        | Leu        | Leu        | Glu<br>480 |
| Gly         | Asn        | Pro        | Gly        | Pro        | Pro         | Ala        | Asp        | Pro        | Asp        | Gly        | Gly        | Pro        | Arg        | Pro        | Gln        |



Ala Asp Arg Lys Phe Gln Glu Arg Glu Val Pro Cys His Arg Pro Ser 500 505 510

Pro Gly Ala Leu Trp Leu Gin Val Ala Val Thr Gly Val Leu Val Val 515 520 525

Thr Leu Leu Val Val Leu Tyr Arg Arg Arg Leu His 530 535 540

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gggaaggagg cagggcaagg ccgggcttgg gggcaggtgg tccgggcatc cagccttgaa 240

gcc gcc cgc cag ctg ggc ctg ctg gtt gac ctc tcc cca gat ggc ctg 337 Ala Ala Arg Gln Leu Gly Leu Leu Val Asp Leu Ser Pro Asp Gly Leu 20 25 30

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ttg gct ttg gtc ggg ggc cag ccc cca gcc ctg gag aag ctc aaa ggc 433 Leu Ala Leu Val Gly Gly Gln Pro Pro Ala Leu Glu Lys Leu Lys Gly 50 55 60

aaa ggt ccc ttg ccg atg gag gcc att gag aag atg gcc agc ctg tgc 481 Lys Gly Pro Leu Pro Met Glu Ala IIe Glu Lys Met Ala Ser Leu Cys 65 70 75 80

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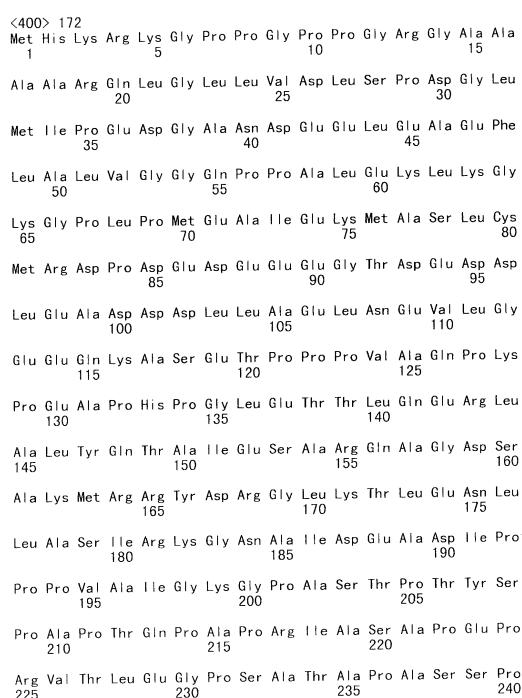
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|------------|-------------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|-------------------|------------|------------|-------------------|------------|------|
| cct<br>Pro | gag<br>Glu<br>130 | gcc<br>Ala | cct<br>Pro | cat<br>His | ccg<br>Pro | ggg<br>Gly<br>135 | ctg<br>Leu | gag<br>Glu | acc<br>Thr | acc<br>Thr | ttg<br>Leu<br>140 | cag<br>Gln | gag<br>Glu | agg<br>Arg        | ctg<br>Leu | 673  |
|            | Leu               |            |            |            |            |                   |            |            |            |            |                   |            |            | gac<br>Asp        |            | 721  |
|            |                   |            |            |            |            |                   |            |            |            |            |                   |            |            | aac<br>Asn<br>175 |            | 769  |
|            |                   |            |            |            |            |                   |            |            |            |            |                   |            |            | atc<br>lle        |            | 817  |
|            |                   |            |            |            |            |                   |            |            |            |            |                   |            |            | tac<br>Tyr        |            | 865  |
|            |                   |            |            |            |            |                   |            |            |            |            |                   |            |            | gag<br>Glu        |            | 913  |
|            |                   |            |            |            |            |                   |            |            |            |            |                   |            |            | tct<br>Ser        |            | 961  |
|            |                   |            |            |            |            |                   |            |            |            |            |                   |            |            | ggc<br>Gly<br>255 |            | 1009 |
|            |                   |            |            |            |            |                   |            |            |            |            |                   |            |            | gcc<br>Ala        |            | 1057 |
|            |                   |            |            |            |            |                   |            |            |            |            |                   |            |            | ttc<br>Phe        |            | 1105 |
|            |                   |            |            |            |            |                   |            |            |            |            |                   |            |            | ggt<br>Gly        |            | 1153 |
|            |                   |            |            |            |            |                   |            |            |            |            |                   |            |            | ccc<br>Pro        |            | 1201 |
|            |                   |            |            |            |            |                   |            | Pro        |            |            |                   |            |            | gcg<br>Ala<br>335 |            | 1249 |
| tcc        | aca               | aca        | gag        | gtg        | ссс        | сса               | ссс        | ccg        | agg        | асс        | ctg               | ctg        | gag        | gcg               | ctg        | 1297 |

| Ser | Thr               | Thr | Glu<br>340 | Va | O <sub>o</sub> | Pro | Pro | Pro<br>345 | Arg | Thr | Leu | Leu | 350 | Ala | Leu |      |
|-----|-------------------|-----|------------|----|----------------|-----|-----|------------|-----|-----|-----|-----|-----|-----|-----|------|
|     | cag<br>G n        |     |            |    |                |     |     |            |     |     |     |     |     |     |     | 1345 |
|     | ggg<br>Gly<br>370 |     |            |    |                |     |     |            |     |     |     |     |     |     |     | 1393 |
|     | caa<br>Gln        |     |            |    |                |     |     |            |     |     |     |     |     |     |     | 1441 |
|     | gaa<br>Glu        |     |            |    |                |     |     |            |     |     |     |     |     |     |     | 1489 |
|     | acc<br>Thr        |     |            |    |                |     |     |            |     |     |     |     |     |     |     | 1537 |
|     | aag<br>Lys        |     |            |    |                |     |     |            |     |     |     |     |     |     |     | 1585 |
|     | cct<br>Pro<br>450 |     |            |    |                |     |     |            |     |     |     |     |     |     |     | 1633 |
|     | cca<br>Pro        |     |            |    |                |     |     |            |     |     |     |     |     |     |     | 1681 |
|     | ccc<br>Pro        |     |            |    |                |     |     |            |     |     |     |     |     |     |     | 1729 |
|     | gag<br>Glu        |     |            |    |                |     |     |            |     |     |     |     |     |     |     | 1777 |
|     | aaa<br>Lys        |     |            |    |                |     |     |            |     |     |     |     |     |     |     | 1825 |
|     | ctg<br>Leu<br>530 |     |            |    |                |     |     |            |     |     |     |     |     |     |     | 1873 |
|     | acc<br>Thr        |     |            |    |                |     |     |            |     |     |     |     |     |     |     | 1921 |
|     | cag<br>G n        |     |            |    |                |     |     |            |     |     |     |     |     |     |     | 1969 |

|            | gaa<br>Glu        |                   |            |            |            |            |                   |            |            |            |            |                   |            |            |            | 2017 |
|------------|-------------------|-------------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------|
|            | tca<br>Ser        |                   |            |            |            |            |                   |            |            |            |            |                   |            |            |            | 2065 |
|            | gaa<br>Glu<br>610 |                   |            |            |            |            |                   |            |            |            |            |                   |            |            |            | 2113 |
|            | gcc<br>Ala        |                   |            |            |            |            |                   |            |            |            |            |                   |            |            |            | 2161 |
|            | acc<br>Thr        |                   |            |            |            |            |                   |            |            |            |            |                   |            |            |            | 2209 |
|            | ctc<br>Leu        |                   |            |            |            |            |                   |            |            |            |            |                   |            |            |            | 2257 |
|            | tcc<br>Ser        |                   |            |            |            |            |                   |            |            |            |            |                   |            |            |            | 2305 |
|            | aac<br>Asn<br>690 |                   |            |            |            |            |                   |            |            |            |            |                   |            |            |            | 2353 |
|            | gac<br>Asp        |                   |            |            |            |            |                   |            |            |            |            |                   |            |            |            | 2401 |
|            | cac<br>His        |                   |            |            |            |            |                   |            |            |            |            |                   |            |            |            | 2449 |
|            | gtg<br>Val        |                   |            |            |            |            |                   |            |            |            |            |                   |            |            |            | 2497 |
| aca<br>Thr | gcc<br>Ala        | cag<br>Gln<br>755 | ctg<br>Leu | aag<br>Lys | ctg<br>Leu | gat<br>Asp | gca<br>Ala<br>760 | ctg<br>Leu | gag<br>Glu | ata<br>Ile | gca<br>Ala | tgt<br>Cys<br>765 | gag<br>Glu | gtc<br>Val | cgg<br>Arg | 2545 |
|            | atc<br>Ile<br>770 |                   |            |            |            |            |                   |            |            |            |            |                   |            |            |            | 2593 |
|            | gta<br>Val        |                   |            |            |            |            |                   |            |            |            |            |                   |            |            |            | 2641 |
| acg        | acg               | aca               | gag        | agg        | tgg        | ctg        | gtc               | att        | gac        | cct        | gtg        | ccg               | gca        | gct        | gtg        | 2689 |

|    |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | _                 |                   |                   | _                 |                   |                   |      |
|----|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
|    | Thr               | Thr               | Thr               | Glu               | A<br>805          | rp                | Leu               | Val               | lle               | Asp<br>810        | Pro               | Val               | Pro               |                   | Ala<br>815        | Val               |      |
|    | ccc<br>Pro        | aca<br>Thr        | cag<br>Gln        | gtt<br>Val<br>820 | gct<br>Ala        | ggg<br>Gly        | ccc<br>Pro        | aaa<br>Lys        | ggg<br>Gly<br>825 | aag<br>Lys        | gcc<br>Ala        | cct<br>Pro        | cct<br>Pro        | gtg<br>Val<br>830 | cct<br>Pro        | gcc<br>Ala        | 2737 |
| o. | cct<br>Pro        | gca<br>Ala        | agg<br>Arg<br>835 | gag<br>Glu        | tca<br>Ser        | ggg<br>Gly        | aac<br>Asn        | aga<br>Arg<br>840 | tca<br>Ser        | gcc<br>Ala        | cgg<br>Arg        | ccc<br>Pro        | ctg<br>Leu<br>845 | cat<br>His        | agc<br>Ser        | ctc<br>Leu        | 2785 |
|    | agt<br>Ser        | gtg<br>Val<br>850 | ctg<br>Leu        | gcg<br>Ala        | ttt<br>Phe        | gac<br>Asp        | caa<br>Gln<br>855 | gag<br>Glu        | cgt<br>Arg        | ctg<br>Leu        | gag<br>Glu        | cgg<br>Arg<br>860 | aag<br>Lys        | atc<br>Ile        | ctg<br>Leu        | gcc<br>Ala        | 2833 |
|    | ctc<br>Leu<br>865 | agg<br>Arg        | cag<br>Gln        | gcg<br>Ala        | cgg<br>Arg        | cgg<br>Arg<br>870 | ccg<br>Pro        | gtg<br>Val        | ccc<br>Pro        | cca<br>Pro        | gaa<br>Glu<br>875 | gtg<br>Val        | gcc<br>Ala        | cag<br>Gln        | cag<br>Gln        | tac<br>Tyr<br>880 | 2881 |
|    | cag<br>Gln        | gac<br>Asp        | atc<br>lle        | atg<br>Met        | caa<br>Gln<br>885 | cgc<br>Arg        | agc<br>Ser        | cag<br>Gln        | tgg<br>Trp        | cag<br>Gln<br>890 | agg<br>Arg        | gca<br>Ala        | cag<br>Gln        | ctg<br>Leu        | gag<br>Glu<br>895 | cag<br>Gln        | 2929 |
|    | ggg<br>Gly        | ggt<br>Gly        | gtg<br>Val        | ggc<br>Gly<br>900 | atc<br>lle        | cga<br>Arg        | cgg<br>Arg        | gaa<br>Glu        | tac<br>Tyr<br>905 | aca<br>Thr        | gcc<br>Ala        | cag<br>Gln        | ctg<br>Leu        | gag<br>Glu<br>910 | cgg<br>Arg        | cag<br>Gln        | 2977 |
|    | ctg<br>Leu        | cag<br>Gln        | ttc<br>Phe<br>915 | tac<br>Tyr        | acg<br>Thr        | gag<br>Glu        | gct<br>Ala        | gcc<br>Ala<br>920 | cgg<br>Arg        | cgc<br>Arg        | ctg<br>Leu        | ggc<br>Gly        | aac<br>Asn<br>925 | gat<br>Asp        | ggc<br>Gly        | agc<br>Ser        | 3025 |
|    | agg<br>Arg        | gat<br>Asp<br>930 | gct<br>Ala        | gca<br>Ala        | aag<br>Lys        | gag<br>Glu        | gcg<br>Ala<br>935 | ctc<br>Leu        | tat<br>Tyr        | agg<br>Arg        | cgg<br>Arg        | aat<br>Asn<br>940 | ctg<br>Leu        | gta<br>Val        | ggg<br>Gly        | agt<br>Ser        | 3073 |
|    | Glu               | Leu               | Gln               | Arg               | ctc<br>Leu        | Arg               | Arg               | tga               | ggago             | ccc a             | atgg              | ggcg              | gg ca             | agcc              | ccca              | g                 | 3124 |
|    | aaag              | gcggg             | gca į             | gcag              | gccc              | cg a              | tacc              | ggga              | a ga              | gccga             | acac              | agc               | cacga             | aac               | caga              | caagca            | 3184 |
|    | gaca              | aatca             | agc (             | ggac              | aatc              | gg t              | tctg              | gact              | c ac              | ccct              | catc              | cgg               | gccc              | сса               | gccc              | cgccag            | 3244 |
|    | agco              | ctcc              | gtg               | gctg              | cggg              | tg t              | tggg              | aacc              | a tg              | cctg              | ccag              | cca               | gtat              | gtg               | cccc              | tcaccc            | 3304 |
|    | aggo              | cctg              | gct               | gggc              | cctg              | ga g              | agto              | ctgt              | t tg              | caca              | gccc              | agg               | ggtg              | tcc               | ggcc              | tctggc            | 3364 |
|    | ccg               | ccc               | gga               | gcag              | ggag              | gg c              | ggct              | gggg              | c ca              | agcc              | ccga              | ggg               | cccc              | tgc               | aagc              | acttta            | 3424 |
|    | ctt               | cctg              | ttc               | ctcc              | ccag              | cc t              | taac              | ccca              | a ag              | ccct              | cctg              | cac               | ссса              | aag               | aagc              | cactga            | 3484 |
|    | ggc               | tggc              | cga               | gcca              | cact              | gt c              | tccc              | cagg              | g gc              | gtcg              | acct              | ggc               | ccag              | ctg               | ggtc              | cccagg            | 3544 |
|    | cca               | gcac              | atg               | gaat              | aaaa <sup>.</sup> | ta g              | ccag              | ggcc              | a ca              | ctc               |                   |                   |                   |                   |                   |                   | 3579 |

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Gly Leu Ala Lys Pro Gln Met Pro Pro Gly Pro Cys Ser Pro Gly Pro 255

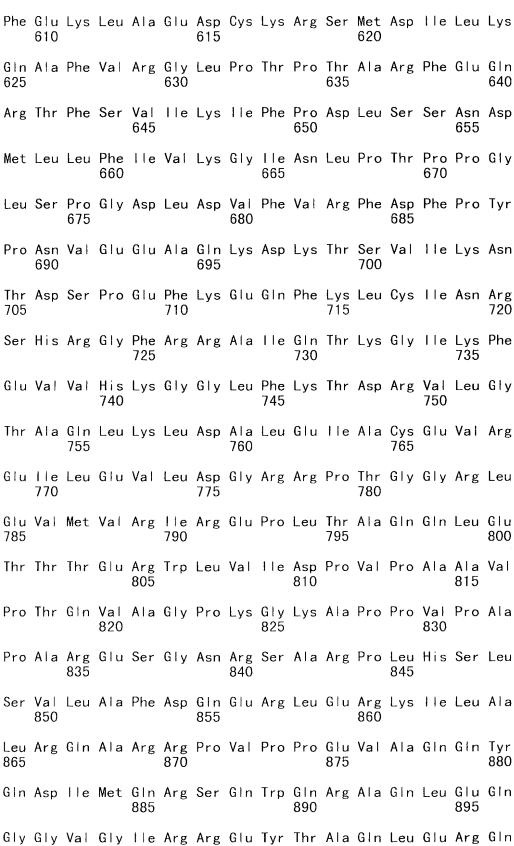
Leu Ala Gln Leu Gln Ser Arg Gln Arg Asp Tyr Lys Leu Ala Ala Leu 260

His Ala Lys Gln Gln Gly Asp Thr Thr Ala Ala Ala Arg His Phe Arg

280

| /al        | Ala<br>290 | Lys        | Ser          | PI         | sp         | Ala<br>295 | Val        | Leu          | Glu        | Ala          | Leu<br>300   | Ser        |              | Gly        | Glu         |
|------------|------------|------------|--------------|------------|------------|------------|------------|--------------|------------|--------------|--------------|------------|--------------|------------|-------------|
| Pro<br>305 | Val        | Asp        | Leu          | Ser        | Cys<br>310 | Leu        | Pro        | Pro          | Pro        | Pro<br>315   | Asp          | Gln        | Leu          | Pro        | Pro<br>320  |
| Asp        | Pro        | Pro        | Ser          | Pro<br>325 | Pro        | Ser        | Gln        | Pro          | Pro<br>330 | Thr          | Pro          | Ala        | Thr          | Ala<br>335 | Pro         |
| Ser        | Thr        | Thr        | G u<br>340   | Val        | Pro        | Pro        | Pro        | Pro<br>345   | Arg        | Thr          | Leu          | Leu        | Glu<br>350   | Ala        | Leu         |
| Glu        | Gln        | Arg<br>355 | Met          | Glu        | Arg        | Tyr        | Gln<br>360 | Val          | Ala        | Ala          | Ala          | Gln<br>365 | Ala          | Lys        | Ser         |
| Lys        | Gly<br>370 | Asp        | Gln          | Arg        | Lys        | Ala<br>375 | Arg        | Met          | His        | Glu          | Arg<br>380   | lle        | Val          | Lys        | Gln         |
| Tyr<br>385 | Gln        | Asp        | Ala          | He         | Arg<br>390 | Ala        | His        | Lys          | Ala        | Gly<br>395   | Arg          | Ala        | Val          | Asp        | Va l<br>400 |
| Ala        | Glu        | Leu        | Pro          | Val<br>405 | Pro        | Pro        | Gly        | Phe          | Pro<br>410 | Pro          | lle          | Gln        | Gly          | Leu<br>415 | Glu         |
| Ala        | Thr        | Lys        | Pro<br>420   | Thr        | Gln        | Gln        | Ser        | Leu<br>425   | Val        | Gly          | Val          | Leu        | G1u<br>430   | Thr        | Ala         |
| Met        | Lys        | Leu<br>435 | Ala          | Asn        | Gln        | Asp        | G u<br>440 | Gly          | Pro        | Glu          | Asp          | Glu<br>445 | Glu          | Asp        | Glu         |
| Val        | Pro<br>450 | Lys        | Lys          | Gln        | Asn        | Ser<br>455 | Pro        | Val          | Ala        | Pro          | Thr<br>460   | Ala        | Gln          | Pro        | Lys         |
| Ala<br>465 |            | Pro        | Ser          | Arg        | Thr<br>470 | Pro        | Gln        | Ser          | Gly        | Ser<br>475   | Ala          | Pro        | Thr          | Ala        | Lys<br>480  |
| Ala        | Pro        | Pro        | Lys          | Ala<br>485 | Thr        | Ser        | Thr        | Arg          | Ala<br>490 | Gln          | Gln          | Gln        | Leu          | Ala<br>495 | Phe         |
| Leu        | Glu        | Gly        | Arg<br>500   |            | Lys        | Gln        | Leu        | Leu<br>505   | Gln        | Ala          | Ala          | Leu        | Arg<br>510   | Ala        | Lys         |
| Gln        | Lys        | Asn<br>515 |              | Val        | Glu        | Gly        | Ala<br>520 | Lys<br>)     | Met        | : His        | Leu          | Arg<br>525 | Gln          | Ala        | Lys         |
| Gly        | Leu<br>530 |            | ı Pro        | Met        | Leu        | G1u<br>535 | ı Ala      | ser          | Arg        | g Asr        | 6 Gly<br>540 | Leu        | Pro          | Val        | Asp         |
| 11e<br>545 |            | · Lys      | ; Val        | Pro        | Pro<br>550 | Ala        | a Pro      | val          | Asr        | 1 Lys<br>555 | Asp<br>5     | Asp        | Phe          | Ala        | Leu<br>560  |
| Val        | Glr        | n Arg      | g Pro        | Gly<br>565 | Pro        | Gly        | / Leu      | ı Ser        | Glr<br>570 | n Glu        | ı Ala        | a Ala      | Arg          | 575<br>575 | y Tyr       |
| Gly        | / Glu      | ı Lei      | 1 Thr<br>580 | · Lys      | s Lei      | ılle       | e Arg      | g Glr<br>585 | Glr<br>5   | n His        | s Glu        | ı Met      | : Cys<br>590 | Leu<br>)   | ı Asn       |
| His        | s Sei      | r Asr      | n Glr        | n Phe      | e Thr      | Gli        | n Lei      | ı Gly        | / Asr      | n He         | e Thr        | Glu        | ı Thr        | - Thi      | Lys         |







Leu Gln Phe Tyr Thr Glu Ala Ala Arg Arg Leu Gly Asn Asp Gly Ser 915 920 925

Arg Asp Ala Ala Lys Glu Ala Leu Tyr Arg Arg Asn Leu Val Gly Ser 930 935 940

Glu Leu Gln Arg Leu Arg Arg 945 950

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Met Gly Asp Arg Arg Phe lle

aat gca act gcc aat aat act tgc att gtt gat gat tcc ttc aag tat 690 Asn Ala Thr Ala Asn Asn Thr Cys lle Val Asp Asp Ser Phe Lys Tyr 25 30 35

aat ttg aat ggt gct gtc tat agt gtt gta ttc atc ctg ggt cta ata 738 Asn Leu Asn Gly Ala Val Tyr Ser Val Val Phe Ile Leu Gly Leu Ile 40 45 50 55

acc aac agt gcc tcc ctg ttt gtc ttc tgc ttc cgc atg aaa atg aga 786 Thr Asn Ser Ala Ser Leu Phe Val Phe Cys Phe Arg Met Lys Met Arg

|            |                   |            |            |                   | ttc<br>Phe        |                   |            |            |                   |            |                   |            |            |                   |            | 834  |
|------------|-------------------|------------|------------|-------------------|-------------------|-------------------|------------|------------|-------------------|------------|-------------------|------------|------------|-------------------|------------|------|
|            |                   |            |            |                   | cct<br>Pro        |                   |            |            |                   |            |                   |            |            |                   |            | 882  |
|            |                   |            |            |                   | acc<br>Thr        |                   |            |            |                   |            |                   |            |            |                   |            | 930  |
|            |                   |            |            |                   | agc<br>Ser<br>125 |                   |            |            |                   |            |                   |            |            |                   |            | 978  |
| cgt<br>Arg | ttc<br>Phe        | cta<br>Leu | gcc<br>Ala | att<br>  e<br>140 | gtc<br>Val        | tat<br>Tyr        | ccc<br>Pro | ttc<br>Phe | cga<br>Arg<br>145 | tcg<br>Ser | cgt<br>Arg        | acc<br>Thr | atc<br>lle | agg<br>Arg<br>150 | acc<br>Thr | 1026 |
|            |                   |            |            |                   | att<br>Ile        |                   |            |            |                   |            |                   |            |            |                   |            | 1074 |
|            |                   |            |            |                   | gct<br>Ala        |                   |            |            |                   |            |                   |            |            |                   |            | 1122 |
| gcg<br>Ala | acc<br>Thr<br>185 | acc<br>Thr | act<br>Thr | tgc<br>Cys        | ttt<br>Phe        | gaa<br>Glu<br>190 | ggc<br>Gly | ttc<br>Phe | tcc<br>Ser        | aaa<br>Lys | cgt<br>Arg<br>195 | gtc<br>Val | tgg<br>Trp | aag<br>Lys        | aca<br>Thr | 1170 |
|            |                   |            |            |                   | act<br>Thr<br>205 |                   |            |            |                   |            |                   |            |            |                   |            | 1218 |
|            |                   |            |            |                   | gtt<br>Val        |                   |            |            |                   |            |                   |            |            |                   |            | 1266 |
|            |                   |            |            |                   | ttg<br>Leu        |                   |            |            |                   |            |                   |            |            |                   |            | 1314 |
|            |                   |            |            |                   | gtg<br>Val        |                   |            |            |                   |            |                   |            |            |                   |            | 1362 |
|            |                   |            |            |                   | ctc<br>Leu        |                   |            |            |                   |            |                   |            |            |                   |            | 1410 |
|            |                   |            |            |                   | ttg<br>Leu<br>285 |                   |            |            |                   |            |                   |            |            |                   |            | 1458 |

| acc ttg tg<br>Thr Leu Cy | c ctt gca<br>s Leu Ala 7<br>300 | t ctg aat<br>hr Leu Asn | tgt tgc ttt<br>Cys Cys Phe<br>305 | gat cct t<br>Asp Pro Ph | itc tat<br>e lle Tyr<br>310 | 1506 |
|--------------------------|---------------------------------|-------------------------|-----------------------------------|-------------------------|-----------------------------|------|
|                          |                                 |                         | aag toc ttt<br>Lys Ser Phe<br>320 |                         | n Thr His                   | 1554 |
|                          | t Glu Ser L                     |                         | act gag aca<br>Thr Glu Thr        |                         |                             | 1602 |
|                          |                                 |                         | gaa gtt agt<br>Glu Val Ser        |                         |                             | 1650 |
|                          | y Glu Leu M                     |                         | tcc acc ttc<br>Ser Thr Phe<br>370 |                         | aattgtcttt                  | 1703 |
| caggttcagc               | tacagtgtct                      | cttatgatt               | t ttttcctatg                      | ctataaatag              | gagaaacaaa                  | 1763 |
| ttgaagctaa               | tgatactgag                      | aatagagta               | a tgtaccaaat                      | gcagtcagat              | acatttgttt                  | 1823 |
| gaacactatt               | gtacatatto                      | tgttttgtt               | c agtaattata                      | ggtcaagtct              | aattacaaca                  | 1883 |
| accaaaacag               | atcagcctct                      | tctgttgag               | t tgacttttca                      | ttacctaaat              | gaccagtggt                  | 1943 |
| cttgactttt               | agtgatgtga                      | gggttattt               | t taaacttaaa                      | aaaaaaggca              | ttccagtaat                  | 2003 |
| tttggtaatt               | gggttgggcc                      | tataaatat               | a gaacaaattc                      | agggattatt              | taaaaacatc                  | 2063 |
| tgtgttacta               | ctgatatatg                      | ctagtattt               | t tttccttttt                      | tgaattaata              | ttgaatttat                  | 2123 |
| tttaaaaaaaa              | gaactatttt                      | tacctaatc               | t taataagaca                      | tactgagaaa              | gagaaatgtg                  | 2183 |
| ttgaatttta               | aaatattggc                      | aaattttac               | c tagatttaa                       | aaacctaaat              | gaagtgtttg                  | 2243 |
| aatgaatatg               | ggtgggaaat                      | ttggaattt               | a gacaacattt                      | acgcatttat              | aataaccaca                  | 2303 |
| attagtgtca               | gcttttaaaa                      | ctttctttt               | t aaaataattc                      | tagaattttc              | atatgaaatt                  | 2363 |
| gttaatcctg               | aaaggtgcta                      | cttatgtgc               | c tggcaggtat                      | aaaatggaaa              | actcataaaa                  | 2423 |
| ttaacagtgt               | caatttaaaa                      | aaaaaaaaa               | c tttaagcaac                      | actatattat              | ttcttaagat                  | 2483 |
| tttcatttat               | cctttatggg                      | ggtggggat               | t ggcttgtaga                      | aaatatttat              | tcttcatgtt                  | 2543 |
| aaatgttggg               | gacacattac                      | agccagaga               | g ctacagtatt                      | tgtgcccagg              | tcaggagtaa                  | 2603 |
| attgaaaaag               | taagtgaata                      | gaatagtag               | c agcaagatat                      | cttagagctt              | atattagtag                  | 2663 |
| tttttaaggt               | ggtggttaga                      | tagctgtaa               | t tttgaaatcc                      | atactctctt              | ctgtacattt                  | 2723 |
| tggagcacat               | tgtagccaag                      | gcgctgctg               | a atttgtgctc                      | aggtcgggag              | catattgaaa                  | 2783 |
| aagatgtgta               | cat                             |                         |                                   |                         |                             | 2796 |

|            |             |            | sapi       | ens        |            |            |            |            |            |            |            |            |            |            |            |
|------------|-------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
|            | 0> 1<br>Gly |            | Arg        | Arg<br>5   | Phe        | lle        | Asp        | Phe        | GIn<br>10  | Phe        | Gln        | Asp        | Leu        | Asn<br>15  | Ser        |
| Ser        | Leu         | Arg        | Pro<br>20  | Arg        | Leu        | Gly        | Asn        | Ala<br>25  | Thr        | Ala        | Asn        | Asn        | Thr<br>30  | Cys        | Hε         |
| Val        | Asp         | Asp<br>35  | Ser        | Phe        | Lys        | Tyr        | Asn<br>40  | Leu        | Asn        | Gly        | Ala        | Va I<br>45 | Tyr        | Ser        | Val        |
| Val        | Phe<br>50   | He         | Leu        | Gly        | Leu        | 11e<br>55  | Thr        | Asn        | Ser        | Ala        | Ser<br>60  | Leu        | Phe        | Val        | Phe        |
| Cys<br>65  | Phe         | Arg        | Met        | Lys        | Met<br>70  | Arg        | Ser        | Glu        | Thr        | Ala<br>75  | Thr        | Phe        | Пe         | Thr        | Asr<br>80  |
| Leu        | Ala         | Leu        | Ser        | Asp<br>85  | Leu        | Leu        | Phe        | Val        | Cys<br>90  | Thr        | Leu        | Pro        | Phe        | Lys<br>95  | Πte        |
| Phe        | Tyr         | Asn        | Phe<br>100 | Asn        | Arg        | His        | Trp        | Pro<br>105 | Phe        | Gly        | Asp        | Thr        | Leu<br>110 | Cys        | Lys        |
| lle        | Ser         | Gly<br>115 | Thr        | Ala        | Phe        | Leu        | Thr<br>120 | Asn        | He         | Tyr        | Gly        | Ser<br>125 | Met        | Leu        | Phe        |
| Leu        | Thr<br>130  | Cys        | He         | Ser        | Val        | Asp<br>135 | Arg        | Phe        | Leu        | Ala        | 11e<br>140 | Val        | Tyr        | Pro        | Phe        |
| Arg<br>145 | Ser         | Arg        | Thr        | lle        | Arg<br>150 | Thr        | Arg        | Arg        | Asn        | Ser<br>155 | Ala        | lle        | Val        | Cys        | Ala<br>160 |
| Gly        | Val         | Trp        | lle        | Leu<br>165 | Val        | Leu        | Ser        | Gly        | Gly<br>170 | lle        | Ser        | Ala        | Ser        | Leu<br>175 | Phe        |
| Ser        | Thr         | Thr        | Asn<br>180 | Val        | Asn        | Asn        | Ala        | Thr<br>185 | Thr        | Thr        | Cys        | Phe        | Glu<br>190 | Gly        | Phe        |
| Ser        | Lys         | Arg<br>195 | Val        | Trp        | Lys        | Thr        | Tyr<br>200 | Leu        | Ser        | Lys        | Пe         | Thr<br>205 | He         | Phe        | Πe         |
| Glu        | Va l<br>210 | Val        | Gly        | Phe        | Пе         | 11e<br>215 | Pro        | Leu        | lle        | Leu        | Asn<br>220 | Val        | Ser        | Cys        | Ser        |
| Ser<br>225 | Val         | Val        | Leu        | Arg        | Thr<br>230 | Leu        | Arg        | Lys        | Pro        | Ala<br>235 | Thr        | Leu        | Ser        | Gln        | 11e<br>240 |
| Gly        | Thr         | Asn        | Lys        | Lys<br>245 | Lys        | Val        | Leu        | Lys        | Met<br>250 | lle        | Thr        | Val        | His        | Met<br>255 | Ala        |
| Val        | Phe         | Val        | Val<br>260 | Cys        | Phe        | Val        | Pro        | Tyr<br>265 | Asn        | Ser        | Val        | Leu        | Phe 270    | Leu        | Tyr        |

| Ala              | Leu                            | Val<br>275       | Arg              | Ser                   | n                     | Ala                 | 11e<br>280       | Thr                   | Asn              | Cys              | Leu                | Leu<br>285       | d                     | Arg              | Phe              |     |
|------------------|--------------------------------|------------------|------------------|-----------------------|-----------------------|---------------------|------------------|-----------------------|------------------|------------------|--------------------|------------------|-----------------------|------------------|------------------|-----|
| Ala              | Lys<br>290                     | He               | Met              | Tyr                   | Pro                   | 11e<br>295          | Thr              | Leu                   | Cys              | Leu              | Ala<br>300         | Thr              | Leu                   | Asn              | Cys              |     |
| Cys<br>305       | Phe                            | Asp              | Pro              | Phe                   | 11e<br>310            | Tyr                 | Tyr              | Phe                   | Thr              | Leu<br>315       | Glu                | Ser              | Phe                   | Gln              | Lys<br>320       |     |
| Ser              | Phe                            | Tyr              | lle              | Asn<br>325            | Thr                   | His                 | lle              | Arg                   | Met<br>330       | Glu              | Ser                | Leu              | Phe                   | Lys<br>335       | Thr              |     |
| Glu              | Thr                            | Pro              | Leu<br>340       | Thr                   | Pro                   | Lys                 | Pro              | Ser<br>345            | Leu              | Pro              | Ala                | He               | Gln<br>350            | Glu              | Glu              |     |
| Val              | Ser                            | Asp<br>355       | Gln              | Thr                   | Thr                   | Asn                 | Asn<br>360       | Gly                   | Gly              | Glu              | Leu                | Met<br>365       | Leu                   | Glu              | Ser              |     |
| Thr              | Phe<br>370                     |                  |                  |                       |                       |                     |                  |                       |                  |                  |                    |                  |                       |                  |                  |     |
|                  |                                |                  |                  |                       |                       |                     |                  |                       |                  |                  |                    |                  |                       |                  |                  |     |
| <21<br><21       | 0> 1<br>1> 2<br>2> DI<br>3> He | 299<br>NA        | sapie            | ens                   |                       |                     |                  |                       |                  |                  |                    |                  |                       |                  |                  |     |
| <220             | 0>                             |                  |                  |                       |                       |                     |                  |                       |                  |                  |                    |                  |                       |                  |                  |     |
| <22              | 1> CI<br>2> ((                 |                  | (11              | 76)                   |                       |                     |                  |                       |                  |                  |                    |                  |                       |                  |                  |     |
|                  | 0> 1°<br>accga                 |                  | catag            | gtgto                 | ca ga                 | agtg                | gtgaa            | а ссе                 | cctgo            | cagc             | cago               | caggo            | cct o                 | cctga            | aaaaaa           | 60  |
| aag <sup>.</sup> | tcc a                          | atg g<br>Met (   | ggt g<br>Gly /   | gac a<br>Asp <i>l</i> | aga a<br>Arg <i>l</i> | aga f<br>Arg f<br>5 | ttc a<br>Phe     | att g<br>lle <i>i</i> | gac<br>Asp (     | ttc (<br>Phe (   | caa<br>Gin I<br>10 | ttc (<br>Phe (   | caa g<br>Gln <i>l</i> | gat (<br>Asp (   | ca<br>Ser        | 108 |
| aat<br>Asn<br>15 | tca<br>Ser                     | agc<br>Ser       | ctc<br>Leu       | aga<br>Arg            | ccc<br>Pro<br>20      | agg<br>Arg          | ttg<br>Leu       | ggc<br>Gly            | aat<br>Asn       | gct<br>Ala<br>25 | act<br>Thr         | gcc<br>Ala       | aat<br>Asn            | aat<br>Asn       | act<br>Thr<br>30 | 156 |
| tgc<br>Cys       | att<br>Ile                     | gtt<br>Val       | gat<br>Asp       | gat<br>Asp<br>35      | tcc<br>Ser            | ttc<br>Phe          | aag<br>Lys       | tat<br>Tyr            | aat<br>Asn<br>40 | ctc<br>Leu       | aat<br>Asn         | ggt<br>Gly       | gct<br>Ala            | gtc<br>Val<br>45 | tac<br>Tyr       | 204 |
| agt<br>Ser       | gtt<br>Val                     | gta<br>Val       | ttc<br>Phe<br>50 | atc<br>Ile            | ttg<br>Leu            | ggt<br>Gly          | ctg<br>Leu       | ata<br>Ile<br>55      | acc<br>Thr       | aac<br>Asn       | agt<br>Ser         | gtc<br>Val       | tct<br>Ser<br>60      | ctg<br>Leu       | ttt<br>Phe       | 252 |
| gtc<br>Val       | ttc<br>Phe                     | tgt<br>Cys<br>65 | ttc<br>Phe       | cgc<br>Arg            | atg<br>Met            | aaa<br>Lys          | atg<br>Met<br>70 | aga<br>Arg            | agt<br>Ser       | gag<br>Glu       | act<br>Thr         | gct<br>Ala<br>75 | att<br>He             | ttt<br>Phe       | atc<br>Ile       | 300 |
| acc<br>Thr       | aat                            | cta              | gct              | gtc                   | tct                   | gat                 | ttg              | ctt                   | ttt              | gtc              | tgt                | aca              | cta                   | cct              | ttt              | 348 |

| aaa<br>Lys<br>95  | ata<br>Ile        | ttt<br>Phe        | tac<br>Tyr        | aac<br>Asn        | ttc<br>Phe<br>100 | aac<br>Asn        | cgc<br>Arg        | cac<br>His        | tgg<br>Trp        | cct<br>Pro<br>105 | ttt<br>Phe        | ggt<br>Gly        | gac<br>Asp        | acc<br>Thr        | ctc<br>Leu<br>110 | 396  |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| tgc<br>Cys        | aag<br>Lys        | atc<br>Ile        | tct<br>Ser        | gga<br>Gly<br>115 | act<br>Thr        | gca<br>Ala        | ttc<br>Phe        | ctt<br>Leu        | acc<br>Thr<br>120 | aac<br>Asn        | atc<br>lle        | tat<br>Tyr        | ggg<br>Gly        | agc<br>Ser<br>125 | atg<br>Met        | 444  |
| ctc<br>Leu        | ttt<br>Phe        | ctc<br>Leu        | acc<br>Thr<br>130 | tgt<br>Cys        | att<br>lle        | agt<br>Ser        | gtg<br>Val        | gat<br>Asp<br>135 | cgt<br>Arg        | ttc<br>Phe        | ctg<br>Leu        | gcc<br>Ala        | att<br>11e<br>140 | gtc<br>Val        | tat<br>Tyr        | 492  |
| cct<br>Pro        | ttt<br>Phe        | cga<br>Arg<br>145 | tct<br>Ser        | cgt<br>Arg        | act<br>Thr        | att<br>lle        | agg<br>Arg<br>150 | act<br>Thr        | agg<br>Arg        | agg<br>Arg        | aat<br>Asn        | tct<br>Ser<br>155 | gcc<br>Ala        | att<br>Ile        | gtg<br>Val        | 540  |
| tgt<br>Cys        | gct<br>Ala<br>160 | ggt<br>Gly        | gtc<br>Val        | tgg<br>Trp        | atc<br>Ile        | cta<br>Leu<br>165 | gtc<br>Val        | ctc<br>Leu        | agt<br>Ser        | ggc<br>Gly        | ggt<br>Gly<br>170 | att<br>He         | tca<br>Ser        | gcc<br>Ala        | tct<br>Ser        | 588  |
| ttg<br>Leu<br>175 | ttt<br>Phe        | tcc<br>Ser        | acc<br>Thr        | act<br>Thr        | aat<br>Asn<br>180 | gtc<br>Val        | aac<br>Asn        | aat<br>Asn        | gca<br>Ala        | acc<br>Thr<br>185 | acc<br>Thr        | acc<br>Thr        | tgc<br>Cys        | ttt<br>Phe        | gaa<br>Glu<br>190 | 636  |
| ggc<br>Gly        | ttc<br>Phe        | tcc<br>Ser        | aaa<br>Lys        | cgt<br>Arg<br>195 | gtc<br>Val        | tgg<br>Trp        | aag<br>Lys        | act<br>Thr        | tat<br>Tyr<br>200 | tta<br>Leu        | tcc<br>Ser        | aag<br>Lys        | atc<br>Ile        | aca<br>Thr<br>205 | ata<br>He         | 684  |
| ttt<br>Phe        | att<br>lle        | gaa<br>Glu        | gtt<br>Val<br>210 | gtt<br>Val        | ggg<br>Gly        | ttt<br>Phe        | atc<br>lle        | att<br>Ile<br>215 | cct<br>Pro        | cta<br>Leu        | ata<br>Ile        | ttg<br>Leu        | aat<br>Asn<br>220 | gtc<br>Val        | tct<br>Ser        | 732  |
| tgc<br>Cys        | tct<br>Ser        | tct<br>Ser<br>225 | gtg<br>Val        | gtg<br>Val        | ctg<br>Leu        | aga<br>Arg        | act<br>Thr<br>230 | ctt<br>Leu        | cgc<br>Arg        | aag<br>Lys        | cct<br>Pro        | gct<br>Ala<br>235 | act<br>Thr        | ctg<br>Leu        | tct<br>Ser        | 780  |
| caa<br>Gln        | lle               | G∣y               | Thr               | aat<br>Asn        | Lys               | Lys               | Lys               | Val               | ctg<br>Leu        | Lys               | Met               | atc<br>lle        | aca<br>Thr        | gta<br>Val        | cat<br>His        | 828  |
| atg<br>Met<br>255 | gca<br>Ala        | gtc<br>Val        | ttt<br>Phe        | gtg<br>Val        | gta<br>Val<br>260 | tgc<br>Cys        | ttt<br>Phe        | gta<br>Val        | ccc<br>Pro        | tac<br>Tyr<br>265 | aac<br>Asn        | tct<br>Ser        | gtc<br>Val        | ctc<br>Leu        | ttc<br>Phe<br>270 | 876  |
| ttg<br>Leu        | tat<br>Tyr        | gcc<br>Ala        | ctg<br>Leu        | gtg<br>Val<br>275 | cgc<br>Arg        | tcc<br>Ser        | caa<br>G n        | gct<br>Ala        | att<br>11e<br>280 | act<br>Thr        | aat<br>Asn        | tgc<br>Cys        | ttt<br>Phe        | ttg<br>Leu<br>285 | gaa<br>Glu        | 924  |
| aga<br>Arg        | ttt<br>Phe        | gca<br>Ala        | aag<br>Lys<br>290 | atc<br>Ile        | atg<br>Met        | tac<br>Tyr        | cca<br>Pro        | atc<br>Ile<br>295 | acc<br>Thr        | ttg<br>Leu        | tgc<br>Cys        | ctt<br>Leu        | gca<br>Ala<br>300 | act<br>Thr        | ctg<br>Leu        | 972  |
| aac<br>Asn        | tgt<br>Cys        | tgt<br>Cys<br>305 | ttt<br>Phe        | gac<br>Asp        | cct<br>Pro        | ttc<br>Phe        | atc<br>lle<br>310 | tat<br>Tyr        | tac<br>Tyr        | ttc<br>Phe        | acc<br>Thr        | ctt<br>Leu<br>315 | gaa<br>Glu        | tcc<br>Ser        | ttt<br>Phe        | 1020 |
| cag               | aag               | tcc               | ttc               | tac               | atc               | aat               | gcc               | cac               | atc               | aga               | atg               | gag               | tcc               | ctg               | ttt               | 1068 |

| Gln Lys Ser<br>320                | Phe Tyl   | e Asn<br>325              | Ala Hi           | s lle A | rg Met<br>330          | Glu §              | Leu Phe                     |      |
|-----------------------------------|-----------|---------------------------|------------------|---------|------------------------|--------------------|-----------------------------|------|
| aag act gaa<br>Lys Thr Glu<br>335 | ı Thr Pro | ttg acc<br>Leu Thr<br>340 | aca aa<br>Thr Ly | s Pro S | cc ctt<br>er Leu<br>45 | cca gct<br>Pro Ala | att caa<br>a lle Gln<br>350 | 1116 |
| gag gaa gtg<br>Glu Glu Val        |           |                           |                  |         |                        |                    |                             | 1164 |
| gaa toc acc<br>Glu Ser Thr        |           | tatgag                    | aaatgtg          | ttc agg | tccagat                | atggtt             | tctc                        | 1216 |
| ctataatttt                        | tcctatgct | a taaac                   | taaag a          | tttgaag | ct aatg                | gatactg            | agaataatgc                  | 1276 |
| accaaatcca                        | gtcagatac | a tttgt                   | ttgaa g          | gtatact | gt agag                | tttta              | ttgctgtttt                  | 1336 |
| gttcagtaat                        | tataggtca | a atcta                   | attac a          | acaacca | ag atgg                | gattgcc            | aaactcttct                  | 1396 |
| gcttggttgg                        | aatttcatt | g tatcg                   | catta t          | ccaggtg | gc tagt                | ggcatt             | tgataatata                  | 1456 |
| gagatgactt                        | tgaaacttt | с ааааа                   | ggtat t          | tctattc | ca atga                | atatttg            | gtaattaggt                  | 1516 |
| tgggcctata                        | aatatagaa | c aaatt                   | caggg a          | ttttaa  | aa aatt                | gtgtta             | ctactgatat                  | 1576 |
| atgctagttt                        | tattttatt | t ttttg                   | gactg t          | cattgag | tt tatt                | ttagca             | caagaatatt                  | 1636 |
| tttagcctaa                        | cattattaa | t aagaa                   | atgtg t          | caaattt | tt aaca                | attggta            | aaatatgtta                  | 1696 |
| tgtgcatttt                        | gaaaacaga | a aacaa                   | attgc g          | ttggcat | gt acgt                | gggtgg             | gaagaaaaag                  | 1756 |
| aaaattaaca                        | ggatttaca | c aatta                   | taatc a          | ccagcag | tg tgag                | tttaaa             | aaacttcgtt                  | 1816 |
| gtttttacac                        | caaattaaa | a ttttc                   | atgtc a          | aacttca | aa gcca                | igaaagc            | tgctaaatac                  | 1876 |
| gtgtctggca                        | ggtaaaagc | t ggaaa                   | attac t          | taaaaca | igg aaag               | tgtcaa             | taaaaaaact                  | 1936 |
| tgagcaacac                        | caacatatt | t tttct                   | taaaa t          | gtcacgt | ta tctt                | catttt             | gggaaactag                  | 1996 |
| gttctataaa                        | atatttatc | c tccct                   | gttat a          | ctttgga | igc acag               | gcacagc            | cagaaagggg                  | 2056 |
| ctgcatttgt                        | gcccaggtc | a ggagc                   | aaatt g          | aaaaaaa | aa ataa                | agtaat             | actaaaaaat                  | 2116 |
| caaactataa                        | acccaaaac | a tttat                   | taaaa c          | ctgaatt | aa toot                | ttttgg             | agggaggagt                  | 2176 |
| agagatatat                        | aacctgaaa | a tactt                   | attct t          | tcttatc | ga attt                | tggagc             | ctaatatagc                  | 2236 |
| caggagctgc                        | tgaatttgt | g cccct                   | ggatt g          | gaaccaa | at aaaa                | aaaaaa             | aaaaaaaatt                  | 2296 |
| cct                               |           |                           |                  |         |                        |                    |                             | 2299 |
|                                   |           |                           |                  |         |                        |                    |                             |      |
| <210> 176<br><211> 370            |           |                           |                  |         |                        |                    |                             |      |

<210> 176 <211> 370 <212> PRT <213> Homo sapiens

<400> 176 Met Gly Asp Arg Arg Phe lle Asp Phe Gln Phe Gln Asp Ser Asn Ser Ser Leu Arg Pro Arg Leu Gly Asn Ala Thr Ala Asn Asn Thr Cys Ile Val Asp Asp Ser Phe Lys Tyr Asn Leu Asn Gly Ala Val Tyr Ser Val Val Phe IIe Leu Gly Leu IIe Thr Asn Ser Val Ser Leu Phe Val Phe Cys Phe Arg Met Lys Met Arg Ser Glu Thr Ala lle Phe lle Thr Asn Leu Ala Val Ser Asp Leu Leu Phe Val Cys Thr Leu Pro Phe Lys Ile Phe Tyr Asn Phe Asn Arg His Trp Pro Phe Gly Asp Thr Leu Cys Lys lle Ser Gly Thr Ala Phe Leu Thr Asn lle Tyr Gly Ser Met Leu Phe 120 Leu Thr Cys lle Ser Val Asp Arg Phe Leu Ala lle Val Tyr Pro Phe Arg Ser Arg Thr Ile Arg Thr Arg Arg Asn Ser Ala Ile Val Cys Ala 155 Gly Val Trp Ile Leu Val Leu Ser Gly Gly Ile Ser Ala Ser Leu Phe Ser Thr Thr Asn Val Asn Asn Ala Thr Thr Thr Cys Phe Glu Gly Phe Ser Lys Arg Val Trp Lys Thr Tyr Leu Ser Lys Ite Thr Ite Phe Ite 200 Glu Val Val Gly Phe Ile Ile Pro Leu Ile Leu Asn Val Ser Cys Ser 215 Ser Val Val Leu Arg Thr Leu Arg Lys Pro Ala Thr Leu Ser Gln lle 235 225 230 Gly Thr Asn Lys Lys Val Leu Lys Met lle Thr Val His Met Ala 250 Val Phe Val Val Cys Phe Val Pro Tyr Asn Ser Val Leu Phe Leu Tyr Ala Leu Val Arg Ser Gin Ala Ile Thr Asn Cys Phe Leu Giu Arg Phe Ala Lys lle Met Tyr Pro lle Thr Leu Cys Leu Ala Thr Leu Asn Cys 295 300

| Cys Phe Asp Pro Phe Tle Tyr<br>305 310                              | Tyr Phe Thr                      | Leu Glu Ser<br>315                | Phe Gln Lys<br>320                   |
|---|----------------------------------|-----------------------------------|--------------------------------------|
| Ser Phe Tyr Ile Asn Ala His<br>325                                  | lle Arg Met<br>330               |                                   | Phe Lys Thr<br>335                   |
| Glu Thr Pro Leu Thr Thr Lys<br>340                                  | Pro Ser Leu<br>345               | Pro Ala Ile                       | Gin Glu Glu<br>350                   |
| Val Ser Asp Gln Thr Thr Asn<br>355                                  | Asn Gly Gly<br>360               | Glu Leu Met<br>365                | Leu Glu Ser                          |
| Thr Phe<br>370  |                                  |                                   |                                      |
| <210> 177<br><211> 973<br><212> DNA<br><213> Homo sapiens           |                                  |                                   |                                      |
| <220><br><221> CDS<br><222> (30) (416)                              |                                  |                                   |                                      |
| <400> 177 cagacagcgg cgggcgcagg acgtg                               | cact atg gct<br>Met Ala<br>1     | cgg ggc tcg<br>Arg Gly Ser<br>5   | ctg cgc cgg 53<br>Leu Arg Arg        |
| ttg ctg cgg ctc ctc gtg ctg<br>Leu Leu Arg Leu Leu Val Leu<br>10 15 | Gly Leu Trp                      | ctg gcg ttg<br>Leu Ala Leu<br>20  | ctg cgc tcc 101<br>Leu Arg Ser       |
| gtg gcc ggg gag caa gcg cca<br>Val Ala Gly Glu Gln Ala Pro<br>25 30 | ggc acc gcc<br>Gly Thr Ala       | ccc tgc tcc<br>Pro Cys Ser<br>35  | cgc ggc agc 149<br>Arg Gly Ser<br>40 |
| tcc tgg agc gcg gac ctg gac<br>Ser Trp Ser Ala Asp Leu Asp<br>45    | aag tgc atg<br>Lys Cys Met<br>50 | gac tgc gcg<br>Asp Cys Ala        | tct tgc agg 197<br>Ser Cys Arg<br>55 |
| gcg cga ccg cac agc gac ttc<br>Ala Arg Pro His Ser Asp Phe<br>60    | tgc ctg ggc<br>Cys Leu Gly<br>65 | tgc gct gca<br>Cys Ala Ala        | gca cct cct 245<br>Ala Pro Pro<br>70 |
| gcc ccc ttc cgg ctg ctt tgg<br>Ala Pro Phe Arg Leu Leu Trp<br>75    | ccc atc ctt<br>Pro IIe Leu<br>80 | ggg ggc gct<br>Gly Gly Ala<br>85  | ctg agc ctg 293<br>Leu Ser Leu       |
| acc ttc gtg ctg ggg ctg ctt<br>Thr Phe Val Leu Gly Leu Leu<br>90 95 | ı Ser Gly Phe                    | ttg gtc tgg<br>Leu Val Trp<br>100 | aga cga tgc 341<br>Arg Arg Cys       |
| cgc agg aga gag aag ttc acc<br>Arg Arg Arg Glu Lys Phe Thr          | acc ccc ata<br>Thr Pro lle       | gag gag acc<br>Glu Glu Thr        | ggc gga gag 389<br>Gly Gly Glu       |

ggc tgc cca gct gtg gcg ctg atc cag tgacaatgtg cccctgcca Gly Cys Pro Ala Val Ala Leu lle Gln 125 436

gccggggctc gcccactcat cattcattca tccattctag agccagtctc tgcctccag 496 acgcggcggg agccaagctc ctccaaccac aaggggggtg gggggcggtg aatcacctcc 556 gaggcctggg tccagggttc aggggaacct tccaaggtgt ctggttgccc tgcctctggc 616 tccagaacag aaagggagcc tcacgctggc tcacacaaaa cagctgacac tgactaagga 676 actgcagcat ttgcacaggg gaggggggtg ccctccttcc tagaggccct gggggccagg 736 ctgacttggg gggcagactt gacactaggc cccactcact cagatgtcct gaaattccac 796 cacgggggtc accctgggg gttagggacc tattttaac actaggggc tggcccacta 856 ggagggctgg ccctaagata cagaccccc caactcccca aagcgggag gagatattta 916 ttttggggag agtttggagg ggagggagaa tttattaata aaagaatctt taacttt

<210> 178

<211> 129

<212> PRT

<213> Homo sapiens

<400> 178

Met Ala Arg Gly Ser Leu Arg Arg Leu Leu Arg Leu Leu Val Leu Gly
1 5 10 15

Leu Trp Leu Ala Leu Leu Arg Ser Val Ala Gly Glu Gln Ala Pro Gly 20 25 30

Thr Ala Pro Cys Ser Arg Gly Ser Ser Trp Ser Ala Asp Leu Asp Lys 35 40 45

Cys Met Asp Cys Ala Ser Cys Arg Ala Arg Pro His Ser Asp Phe Cys 50 55 60

Leu Gly Cys Ala Ala Ala Pro Pro Ala Pro Phe Arg Leu Leu Trp Pro 65 70 75 80

lle Leu Gly Gly Ala Leu Ser Leu Thr Phe Val Leu Gly Leu Leu Ser 85 90 95

Gly Phe Leu Val Trp Arg Arg Cys Arg Arg Arg Glu Lys Phe Thr Thr 100 105 110

Pro lle Glu Glu Thr Gly Gly Glu Gly Cys Pro Ala Val Ala Leu lle 115 120 125

Gln

| <210> 179<br><211> 20<br><212> DNA<br><213> Artificial Sequence |    |
|---|----|
| <220><br><223> Description of Artificial Sequence:Primer        |    |
| <400> 179 cttctgctct aaaagctgcg                                 | 20 |
| <210> 180<br><211> 20<br><212> DNA<br><213> Artificial Sequence |    |
| <220><br><223> Description of Artificial Sequence:Primer        |    |
| <400> 180 cgacctgcag ctcgagcaca                                 | 20 |

## FREE TEXT OF SEQUENCE LISTING

SEQ ID NO: 179 and SEQ ID NO: 180 are primers.

## BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a graph showing NF-  $\kappa$  B reporter activity inhibition by the proteasome inhibitor MG132 in Example 3, the axis of abscissa is MG132 concentration and the transversal axis is relative luciferase activity.

## NAME OF THE DOCUMENT: ABSTRACT

## **ABSTRACT**

**PROBLEMS TO BE SOLVED:** Provision of proteins having NF-  $\kappa$  B activity, which are used for diagnosing, treating or preventing diseases associated with the excessive activation or inhibition of NF-  $\kappa$  B.

MEANS TO SOLVE THE PROBLEMS: Using the plasmid pNF  $\kappa$  B-Luc, the cDNA encoding a protein capable of activating NF-  $\kappa$  B has been cloned from the cDNA library constructed from human lung fibroblasts, and the DNA sequence and the deduced amino acid sequence determined. The protein, the DNA encoding the protein, a recombinant vector containing the DNA, and a transformant containing the recombinant vector are useful for screening a substance inhibiting or promoting NF-  $\kappa$  B activation.

FIG.1

